RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

VOL. 30 MAY, 1938 NO. 5

THE PRODUCTION OF X-RAYS OF VERY SHORT WAVE LENGTH[1]

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THANKS to the initiative, vision, and courage of the medical pioneers, the therapeutic application of the x-rays was started very soon after their discovery.

It is interesting to see how rapidly the new knowledge derived from more recent fundamental physical research has been usefully applied to the further development of the art of radiology.

It is also interesting to note the extent to which modern physical science must be invoked to explain the various processes involved in the production, mensuration, and therapeutic application of the x-rays.

If we start with the electrons caroming about under thermal agitation in the filament spiral of the cathode, we first see them liberated thermally and then driven by the electrostatic field, and directed by means of an electrostatic electron lens, toward the target.

During their flight we are unable to keep track of them very satisfactorily For, in accordance with the principle of indeterminacy, we cannot know accurately both the velocity and the position of a given electron at any instant of time, because the energy which the electron would have to give up to signal its position would reduce its velocity.

The kinetic energy of the electron when it reaches the target is proportional to the potential difference between the electrodes. But its velocity does not increase as rapidly as the potential difference, being held down by an increase with velocity of the electron mass, and not allowed to exceed the velocity of light, in accordance with the relativity principle.

The moving electrons behave in some respects like particles and in other respects as a wave motion. They possess kinetic energy in virtue of their motion, which is a corpuscular property, and yet when they strike a thin metal film they are diffracted in identically the same manner as waves and it is possible to calculate a magnitude, the de Broglie wave length, which is inversely proportional to the velocity It is the existence of this dualism in the nature of both energy and matter that has given rise to the most recent development in theoretical physics—that of quantum mechanics.

Arrived at the target, the rapidly moving electron encounters the electric forces due to the electrons and positively charged nuclei of the atoms which go to make up the target metal. It may make a direct hit with a nucleus near the surface of the target in which case its kinetic energy is transformed into a light quantum—in this case an x-ray having the minimum

[1] Presented before the Fifth International Congress of Radiology in Chicago, Sept. 13–17, 1937.

wave length to be obtained with the voltage in question. Or the electron may penetrate the space lattice of the target to some depth with a gradual loss of energy, and then collide head-on with a nucleus, with the consequent production of a light quantum of smaller energy and hence longer x-ray wave length. Or the moving electron may eject an electron from one of the inner shells of some atom, creating a vacancy there which, when filled by an electron dropping into it from an outer shell, will give rise to one of the x-ray spectrum lines characteristic of that particular shell in that particular kind of atom.

We have so far followed the electron from its original position in the cathode across the vacuous space of the tube and into the space lattice of the target. But it must either get back through the external circuit to its starting point in the cathode or some other electron must be caused to take its place there For the mechanism of electron flow through the metallic conductor, we must look to the physicist specializing in this field in which rapid strides have been made during the past few years.

Leaving now the electron and coming to the x-rays resulting from its more or less rapid deceleration we have seen that, owing to the structure of the target, the x-ray beam of necessity is heterogeneous, covering a wide range of wave lengths. By filtration the percentage of the longer wave lengths can be reduced.

As the x-rays pass through matter (the patient, for example), they produce within this matter photoelectrons and Compton recoil electrons. These, in turn, eject other electrons of lower velocity, and it is this last ionizing process to which we must look for physiological effects and for mensuration. A photoelectron is ejected with almost the full energy of the x-ray quantum while a Compton recoil electron receives only a small fraction of this, the balance going into a quantum of scattered x-radiation.

We see then that even our superficial discussion of what is involved in the mechanism of x-ray production, mensuration, and utilization has involved thermionics, electron optics, the indeterminacy principle, relativity, quantum mechanics, the crystal space lattice, the structure of the atom with its nucleus and with its extra-nuclear electrons arranged in definite energy levels, electrical conduction in the solid state, the Compton effect, etc.; in short, a large fraction of our modern physics.

We come now to the development of x-ray generating apparatus. Many of the early radiologists were able technicians and took an active part in the development of what now would be regarded as a feeble source of radiation. With the substitution later by Snook of the transformer and mechanical rectifier for the induction coil and revolving plate static machine which had first been used, the adequacy and dependability of the high voltage power supply were increased to a point where the x-ray tube itself became the limiting factor.

The early hot-cathode high-vacuum x-ray tube shifted the burden to the high voltage generator, as this tube was capable of operating at the full voltage obtainable from the x-ray transformers in use at the time of its advent.

Following the demands of the medical profession, larger rectifiers and transformers, good for 200,000 volts, were built and, in turn, tubes to take all that these generators could deliver.

The urge for still higher voltages came both from the medical profession, for therapy, and from industry, for the radiography of thick metal sections.

So far as the tube was concerned, it had been shown that the most troublesome factor in going to much higher voltages lay in the production of field currents when the potential gradient at the surface of the cathode became too high. It had also been shown that this difficulty could be obviated by the use of multi-section tubes containing a plurality of electrodes, each of which was maintained at the proper potential.

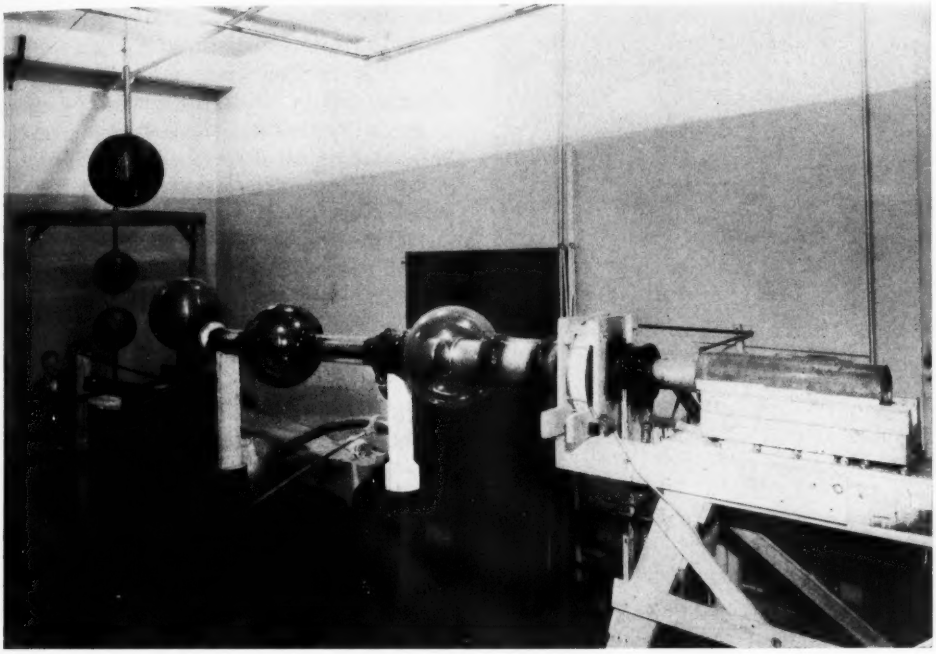

Fig. 1. Early induction-coil x-ray outfit with multi-section tube, used experimentally at voltages up to 900,000 and subsequently used therapeutically for over two years at 700,000 volts.

One of the first experimental outfits which we built for voltages much in excess of 200,000 consisted of a special induction coil with mercury turbine interrupter and a large two-section tube (1). This outfit, shown in Figure 1, operated continuously at 700,000 volts and was tested up to 900,000; it labored under the disadvantages attendant upon the use of a mechanical interrupter.[2]

The operation at the Memorial Hospital, in New York City, for a two- or three-year period of this experimental induction coil outfit was quite educational. It showed, among other things, the desirability, in cases in which continuous pumping of the tube was employed, of having something better than the mercury diffusion pump with its attendant liquid air trap. Away from the laboratory it proved too difficult to maintain the liquid air in the trap for a prolonged period, at the proper level. And when this was not done, the water vapor and carbon dioxide which had been gradually accumulated there in the trap would return to the inner surfaces of the tube to delay the next following operation.

The full appreciation of this difficulty led to the rapid adoption, as soon as it became available, of the oil vapor diffusion pump which required only a water-cooled or a charcoal trap.

Furthermore, the tube was punctured occasionally by operating it at a time when, for one reason or another, the vacuum was too poor. This emphasized the desirability of developing a design which should be puncture-proof no matter what the vacuum and no matter what the electrical characteristics of the high voltage generator.

With transformers, kenotrons, and condensers connected in the Villard circuit, we

[2] Many unsuccessful attempts were made later to develop a circuit in which vacuum tubes could be made to fulfill its function more satisfactorily than did the mechanical interrupter. This was finally accomplished (2), but has not yet been used commercially.

Fig. 2. Oil-immersed induction-coil with multi-section tube.

next developed an 800,000-volt generator and 4-section glass tube combination which has proved very satisfactory in two such installations. These have been operated at 10 ma. but were designed for 30 ma. in case as much intensity as that were desired.

The tube design employed was such that we have never succeeded either in the field or in the laboratory in puncturing the glass envelope. In the laboratory we have taken a single section of this tube which in service has to stand only 200,000 volts and have repeatedly arced it over with 300,000 volts even with heavy condenser discharges, without being able to injure it.

The focusing action in the various sections is such that practically the entire milliamperage leaving the cathode passes through the intermediate electrodes to the anode. The focal spot size is controlled magnetically by a focusing coil.

The tubes in these outfits were originally used without filament bias but with a considerable amount of what might be called geometrical bias incident to focusing. Rose (3) reports that with filament bias on one of these outfits he has been able to raise the r-output per ma. approximately 35 per cent. His absorption curves indicate also a slight increase in hardness with electrostatic filament bias.

Within the above-mentioned limits of voltage and current, the main objections to these outfits are their cost and size, the latter calling for a special building instead of permitting installation in existing hospital rooms.

The facts that tubes can be so designed as to operate just as well on A.C. as on rectified current and to give almost the same quality of radiation on A.C. as on constant potential D.C. lead one to consider very seriously the simple system of a tube connected directly to an A-C source.

One of the least expensive A-C sources is the induction coil, whose operation by the aid of a tube circuit can be made just as regular as that of a transformer. The coil is cheaper than the transformer for two reasons: It requires fewer secondary turns and can be made smaller because of the greater dielectric strength of insulating materials for very steep wave fronts.

In its simplest form, with a straight core, the induction coil has certain disadvantages, however. In the first place its external magnetic field necessitates the use of an insulating tank, and this, in turn, means that for protection from electric shock a considerable amount of space must be kept free around the outfit.

Furthermore, the stray magnetic field introduces a complication in connection with the problem of focusing the tube. We (4) first became acquainted with this in a cathode ray outfit, (see Fig. 2) in which we had mounted a multi-section tube close to an induction coil, connecting the intermediate electrodes of the tube to proper taps in the secondary. The large stray magnetic field of the open core seriously interfered with focusing. Later experiments have shown, however, that a tube placed close to a coil can be so oriented with respect to the coil that the field does not interfere.

On the whole, the disadvantages of the coil over the transformer seem to outweigh the advantages and lead one to choose the latter.

One of our latest developments comprises what seems like a very attractive and in some respects novel type of transformer outfit (5). In this, both tube and high voltage source are in the same grounded metal tank of oil, thus giving complete electrical protection. The outside of such an outfit is shown in Figure 3. The high voltage source is a simple 60-cycle transformer in which the magnetic circuit is opened just enough so that the inductance of the primary, for the frequency in question, balances the capacitance of the secondary. As a result of the electrical tuning secured in this way the power factor is high and the primary current correspondingly low.

Fig. 3. Outside of recently developed oil-immersed 500,000-volt x-ray outfit.

The tube is connected directly to the transformer and must then rectify the current. In the absence of transformer tuning this would result in making the inverse voltage appreciably higher than the useful. With the tuned transformer, however, there are circulating currents in the secondary which are so large compared with the few milliamperes of rectified current supplied to the tube that there is but little difference between the useful and inverse voltages.

The multi-section tube for this outfit is made up of several glass cylinders each $3^1/_2$ inches in diameter and 4 inches long. These are sealed to the metal rings carrying the intermediate electrodes. These metal rings are of Fernico, an alloy which accurately matches in its heat expansion, over a wide temperature range, that of the glass cylinders. The metal extension chamber carrying the target is similarly sealed to the last glass cylinder. We are using 100,000 volts per section. Such tubes are sealed off from the pump, can apparently be made for any voltage, and give promise of having a long life.

Flexibility in the application of the outfit is increased by making the whole tube rotatable about its length axis.

As the target is grounded, it can be cooled with tap water.

An attractive feature of the outfit, in addition to its relatively small size and simplicity, is the accessibility of the target, which, for therapy, can, when desired, be brought very close to the patient, and, for industrial use in metal radiography, be inserted into cavities. This accessibility of the target also makes possible the attainment of x-ray protection with a minimum amount of lead.

The development work on this type of outfit has been as yet largely confined to a size which is being tested in continuous operation at 550,000 volts and 10 ma.

The overall height of the outfit is 4 feet.

The secondary of the transformer consists of a large number, some 76, thin coils. The lower end of the secondary is grounded. The secondary is surmounted by a large hollow metal toroid and the cathode end of the tube is let into this toroid. A few turns of wire within the toroid furnish current to the cathode filament and this current is controlled by a rheostat mounted in e toroid and operated from without by a motor-driven shaft of insulating material. Toroidal metal shells surrounding the tube and electrically connected to the intermediate electrodes shield the tube from the external radial field due to the grounded metal tank.

Outfits of this type can doubtless be developed for higher voltages by increasing the dimensions. Furthermore, various studies which we have under way lead us to

hope that the voltage can be considerably increased, without increase in physical dimensions, by improving the fluid dielectric.

The question of whether it is better to use sealed-off tubes or continuous pumping depends upon various circumstances, as it is one of economics, convenience, and mechanical flexibility. In those cases in which it is merely a matter of economics the answer will depend mainly upon the life of the sealed-off multi-section tube—a factor which is as yet unknown.

I have so far referred largely to the work of our own laboratory and to what are to-day modest voltages—500,000 to 1,000,000.

Succeeding speakers will tell you of other tubes and other types of generator for this voltage range.

For the future attainment of the highest possible voltages two paths are open. One of these, which we owe to Dr. Van de Graaff, will be described by him. The other is the impulse generator, employing the Marx circuit.

The range of the impulse generator has already been carried to 10,000,000 volts and it would apparently be a perfectly straightforward engineering and manufacturing job to build one for several times this voltage. Other things in its favor are the increased electrical strength of insulators for impulses of short over those of long duration and the fact that such generators require no electrostatic shielding from corona, for the simple reason that they make available such large instantaneous current values that corona losses become negligible in comparison.

Brasch and Lange (6) in Germany have used the impulse generator together with a novel type of gas tube for voltages up to 2,400,000.

The disadvantages of the impulse generator for x-ray production would seem to be:

(1) It is not well adapted to use with a hot cathode tube, as for example, to give an average current of a milliampere it would call for a cathode having an emission of perhaps 1,000,000 ma. (Brasch and Lange seem to have been able to get this high emission from the cathode of a gas tube.)

(2) The very high instantaneous energy values make severe mechanical demands on a target, and one would expect to find that a focal spot enormously greater than is now generally used with D.C. or 60-cycle A.C. would be required to give reasonable target life.

With these limitations of the impulse generator type of x-ray outfit in mind, it would seem as though the future production of the shortest possible x-ray wave lengths would be brought about through the use of some form of electrostatic generator and multi-section hot-cathode tube. This seems especially true for the experimental therapeutic application if, as now seems likely, only a milliampere or less of current would be used with such high voltages.

It has been suggested that therapeutic results might be better if enormously greater instantaneous x-ray intensities than are now available were used—intensities of a different order of magnitude, say a million times as great, producing a much greater concentration of ions in the irradiated tissues. If this should be confirmed, some type of condenser machine and gas tube would seem to be indicated. In this connection Dr. Kingdon, of our laboratory, has found that very high instantaneous values of x-ray intensity may be obtained by the discharge of a large condenser through a highly evacuated tube containing a tungsten target and a cathode consisting of liquid mercury maintained at 0° C. (7).

Immediately upon initiation of the discharge through such a tube, mercury vapor is produced by positive ion bombardment of the mercury cathode. This vapor liberation takes place in the path of the discharge, where it is ionized, thus giving rise to further positive ion bombardment of the cathode with the liberation of more electrons and the production of more vapor. This runaway effect is needed to

give the tube sufficient current-carrying capacity, but mustn't be too great as otherwise the voltage will fall off too rapidly with the result that most of the current flow will take place after the voltage has become too low for the production of useful x-rays.

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CALCIFICATION AND OSSIFICATION OF THE KIDNEY

A REVIEW OF THE LITERATURE AND A REPORT OF CASES

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PART I.—INTRODUCTION

ALTHOUGH the literature is replete with many articles dealing with tuberculous calcification of the kidney, relatively little has been written on the subject of non-tuberculous calcification and ossification of the kidney. The majority of text-books and monographs on urology and urological roentgenology fail to mention the occurrence of these conditions and reference to these phenomena is found only in isolated case reports or in cases reported in connection with some other pathological lesion, *i.e.*, cysts, tumors, stones, pyonephrosis, etc.

Our interest in this subject was engendered by several interesting cases which presented calcified shadows in the renal regions in the roentgenogram and offered extremely difficult problems in differential diagnosis. Further impetus was the finding of minute areas of calcification in the kidney which were discernible only on cross-section or microscopic examination of specimens removed at operation for renal lithiasis, pyonephroses, tumors, etc.

For many years calcification has been the subject of much pathological and experimental investigation. In the latter half of the past century, excellent contributions to this subject were made by Virchow, Cohnheim, Czech, Von Kossa, and others. With the dawn of the new century, interest in this fascinating study was stimulated by the notable contributions of Askanazy, Verse, Gierke, Klotz, Tanaka and Katase, and later by the work of Wells, Schmidt, Hofmeister, Lubarsch, and others. In the past few years our knowledge of the chemistry of calcification has been enhanced and extended by the investigations of Howland and his associates on calcium deposits in normal and rachitic bones, and by physico-chemical studies of normal and abnormal changes in the calcium and phosphorus content of tissues and body fluids by Holt, Rabl, Kleinman, Barr, Albright, and others. It is not the intention of the authors to attempt a detailed summation of these studies on calcification in this paper, but rather to present a brief review of the more pertinent facts and theories concerning normal and pathological calcification in general and more specifically to discuss the pathogenesis of calcification in the kidney. Those interested in physiological, physical, and chemical aspects of calcification are referred to the excellent and comprehensive studies of Wells, Schmidt, Barr, Albright, and others.

In the human body, calcification occurs either as a physiologic or pathologic process. Physiological calcification is the normal process concerned with the deposition of calcium salts in the development and the formation of bone. Pathological calcification includes the deposition or precipitation of calcium salts in those tissues or organs which ordinarily do not contain calcium deposits or concrements.

Although several types of pathological calcification have been described, it is extremely difficult to classify them from an etiologic or pathogenic standpoint due to the fact that a precise or satisfactory explanation of the various types of pathological calcification is not always possible or else lacks confirmation and conviction. For practical purposes, we prefer to classify pathological calcification under two main headings, namely, (*a*) metastatic and (*b*) non-metastatic. The distinguishing factor is the fact that in metastatic calcification the deposition of calcium salts presumably takes place in normal or uninjured tissues, whereas the non-metastatic

type of calcification occurs in tissues or organs which are the site of localized changes (*i.e.*, fatty degeneration, hyalinization, degeneration, or necrosis resulting from a toxic, circulatory, or metabolic disturbance) predisposing to the deposition of the calcium salts.

Non-metastatic calcification may be further divided into the following groups, *viz.:* (*a*) dystrophic calcification; (*b*) calcinosis; (*c*) arterial calcification; (*d*) stone formation; (*e*) heterotopic ossification. The latter groups will be briefly discussed only insofar as they concern calcification of the kidney.

Virchow (1855) stressed the etiological relationship of destructive bone diseases to a special type of calcification which he called metastatic calcification (*kalkmetastasen*). His observations were based on eight cases, all but one of which suffered from some destructive bone disease and were accompanied by a varying degree of nephritis; the exception being a case of nephritis unaccompanied by any bone disease. The type of bone disease varied and included osteomyelitis, tuberculous spinal caries, and osseous metastases from a sarcoma of the cheek and an epithelioma of the lip. He showed that the metastatic deposits of calcium salts exhibited a predilection for certain sites, particularly the kidneys, lungs, and stomach and were composed of the same salts which through resorption had disappeared from the bone lesions. He maintained that the important factor governing this abnormal deposition of calcium was the increase in the calcium salts in the blood and that a necessary secondary factor was the presence of a renal lesion which resulted in the faulty excretion of these salts through the kidney, and subsequent deposition in tissues devoid of any previous damage. The importance and significance of hypercalcemia in the production of metastatic calcification has been verified repeatedly in the experimental studies with parathormone and irradiated ergosterol.

It soon became apparent from the reports of Chiari (1878), Hlava (1882), Kockel (1899), Kischensky (1900), Stade (1901), and others that extensive calcification of soft tissues and organs, including the kidneys, occurred in the absence of destructive bone lesions and hypercalcemia, and that other factors undoubtedly played a rôle in the abnormal deposition of calcium. The rôle of nephritis as a primary factor in pathological calcification was emphasized by Schmidt in 1913. He described general calcification with involvement of the kidneys, the so-called *kalkgicht*, in cases of calcium gout without evident bone destruction. He pointed out that the decrease in the solubility of these calcium salts in the blood was caused by a decrease in the amount of albuminous substances in the blood which occurred as a result of the excretion of considerable quantities of albuminous substances by the damaged kidney. The albuminous substances and phosphates normally act as buffers to keep the calcium salts in solution and prevent the precipitation of these salts. Harbitz (1917) and Rabl (1923) also emphasized the rôle of calcium retention and disturbed acid-base equilibrium due to impaired renal function in cases of general calcification without bone destruction.

Dystrophic calcification is the most common type of pathological calcification encountered. It is generally agreed that any dead or damaged tissue, infected or uninfected, so large or so situated that it cannot be absorbed, may become infiltrated with calcium salts. The location and distribution of these calcified lesions are extremely varied inasmuch as every tissue and organ in the body is subject to retrogressive changes or lesions which predispose to the deposition of calcium salts. While it is readily apparent that this type of calcification is directly dependent upon local retrogressive changes, *i.e.*, fatty infiltration, hyalinization, necrosis, etc., which are the result of circulatory, toxic inflammatory or nutritional disturbances, the degree or extent of the calcification may be modified by general changes in calcium metabolism or in the amount of calcium in the blood or tissue fluids.

Kleinman has offered an inclusive theory to explain both the metastatic and dystrophic types of calcification. It is his contention that all calcium deposits in tissues begin with the formation of crystals of tertiary calcium phosphate, and that deposition of these crystals is caused by local or general conditions which produce changes in the calcium and phosphorus concentration and the degree of alkalinity in the blood serum and tissue fluids. The localization of the calcium deposits is determined by the increased alkalinity of certain tissues, *i.e.*, devitalized tissues in cases of dystrophic calcification, and the stomach, lungs, and kidneys in cases of metastatic calcification.

In 1926, Leriche and Policard stated that the deposition of calcium takes place in connective tissue of low metabolism if the blood supply is diminished, particularly in the presence of hypercalcemia. Jones and Roberts (1934) maintained that there is normally a balance between the calcium content and the vascularity of mesenchymatous tissues which they believed was probably associated with phosphatase activity, and that any disturbance in this balance led to pathological changes (calcification) within the affected tissues. Gray (1935) reduced the blood supply to the kidney in rabbits by the ligation of one or more branches of the renal arteries and fed the animals a diet calculated to produce hypercalcemia. He found the deposition of calcium was more marked in the severer grades of renal damage resulting from extensive or total deprivation of blood supply.

The exact physico-chemical changes involved in the deposition of calcium in the various types of pathological calcification remains a matter of conjecture and controversy. As early as 1907, Klotz maintained that calcium deposits occurred as the result of the hydrolysis of fat which resulted in the formation of insoluble calcium soaps. The latter were converted by the action of carbonic acid into calcium phosphate and carbonate with the liberation of fatty acids. In 1911, Wells maintained that pathological calcification was due to either the deposition of calcium salts from the blood directly into the tissues or the precipitation of calcium salts in the excretory or secretory passages of the body. He was of the opinion that the vital factor in pathological calcification was the CO_2 content of the tissues and circulating fluids. He also pointed out that other factors may play a supplementary rôle in calcification, namely, (1) utilization of the proteins of the blood by starving or injured tissue, resulting in a disturbance of the solubility of calcium, and (2) the formulation of a substance or substances, *i.e.*, phosphoric acid, fatty acids, or protein, in the degenerated area having a special affinity for calcium.

In 1923, Robison demonstrated the presence of an active enzyme, phosphatase, in tissues undergoing calcification and ossification such as bone, ossifying cartilage, and tissues, which become the site of calcium deposits such as the kidney. This enzyme aided in the process of calcification by its hydrolyzing effect upon the phosphoric ester which is found in the blood and tissue fluids and whose calcium salt is soluble in plasma and water. The increased concentration of PO_4 ions resulting from the enzyme reaction causes a precipitation of the carbonate molecule. Martland showed that the activity of this enzyme is dependent upon the H-ion concentration of the tissue fluids. He also demonstrated the presence of another phosphatase enzyme in the blood corpuscles and the existence of a delicate balance between the latter enzyme and the H-ion concentration of the tissue fluids. Kay has shown that the kidney possesses a high phosphatase activity which is greater in the cortex than in the medulla. No calcification occurs in the kidney with its high phosphatase activity when the blood calcium is at the normal level, but in the presence of hypercalcemia renal calcification is observed. Kay also pointed out that the phosphatase content of the blood plasma is markedly raised in certain generalized bone diseases, *i.e.*, osteitis

deformans, osteitis fibrosa cystica, osteomalacia, rickets, and renal rickets. In 1934 Rosenheim and Robison were able to produce calcification in the kidney, lung, and aorta *in vitro* by immersing these tissues, freshly excised from normal animals, in solutions containing calcium and inorganic and organic phosphorus. These calcium deposits closely resembled in appearance and distribution those described by Brand and Holtz in 1920, as occurring in experimental hypervitaminosis. In the kidney the calcium deposits *in vitro* were found in the cells and basement membrane of the tubules and were confined to a narrow zone in the cortex, substantiating Kay's observation in the distribution of phosphatase in the kidney.

The extremely variable degree of calcification observed in experimental and clinical conditions with hypercalcemia emphasized the difficulty of attempting to establish a predictable relationship between the degree of hypercalcemia and the deposit of calcium in the tissues. For example, Tanaka and Katase noted only patchy areas of calcification following the intravenous injection of large amounts of calcium, causing a transitory hypercalcemia. Staub observed calcification at or near the site of injection but no calcified changes in distant organs. In experimental ergosterol poisoning, Smith and Elvove obtained variable results, as indicated by the presence of extensive calcium deposits, with only a slight increase in the serum calcium in some cases, and the failure to demonstrate any perceptible increase of calcium in tissues in other cases with hypercalcemia. Shelling obtained calcification of the soft tissues, lungs, and blood vessels in rats with hypocalcemia induced by parathyroidectomy.

From the clinical and experimental evidence at hand it appears that any considerable increase in the concentration of serum phosphatase may disturb the equilibrium of calcium and cause a precipitation of calcium salts. Smith and Elvove found a definite relationship between calcification of the tissues and the phosphate values in the serum in ergosterol poisoning. Albright and his associates found that in hyperparathyroidism the first change was a fall in phosphate values, followed by hypercalcemia, and maintained that these conditions persisted throughout the course of the disease and exerted a favorable influence on the deposition of calcium in the soft tissues.

The Nature of Calcium in the Blood and Tissue Fluids.—From the studies of Klinke, Peters, Van Slyke, and Barr, particularly the latter, we have drawn the following pertinent facts and observations concerning the chemical state of calcium in the body fluids. The normal calcium concentration of human serum varies between 9.0 and 11.5 mgm. per 100 c.c. of serum. This calcium level is not greatly influenced by the injection of calcium salts in large quantities. The injection of parathyroid extract produces hypercalcemia in the absence of any intake of calcium and in spite of the increased excretion of calcium incident to the injection of parathormone. The removal of the parathyroids results in a decrease in the calcium content of the serum, usually to less than one-half of the normal. It appears that parathormone is necessary to keep the calcium values of the tissues at their physiological levels. It is estimated that this hormone is responsible for holding in solution at least from 40 to 50 per cent (4 to 5.8 mgm.) of the normal calcium content of the serum. According to Peters and Eiserson, another portion of the serum calcium, varying between 3 and 4 mgm., is bound to protein. A small amount of serum calcium, less than 25 per cent of the total, remains to be accounted for by the forces ordinarily governing the solubility of calcium in any solution of inorganic salts.

The amount of calcium salts dissolved in serum by the ordinary forces of solubility has been studied by many investigators. Barr has pointed out that analysis of the inorganic substances in tissue fluids indicates that calcium in simple solution exists chiefly in combination with phosphate and carbonate in the form of rela-

tively insoluble salts. Pauli and Samec showed that calcium in the form of calcium phosphate and calcium carbonate is far more soluble in a colloidal albuminous solution than in water. Holt, La Mer, and Chown maintained that neutral calcium phosphate is present in the blood and in saturation up to 200 per cent, but believed that it is transported as the more readily soluble acid carbonate and acid phosphate which are easily converted into the neutral salts. This theory of supersaturation has been substantiated by Sendrey and Hastings but questioned by Klinke and others. Kramer and Shear maintained that the blood serum is actually undersaturated for $Ca\ HPO_4$ and that the calcium and phosphate ions are so combined in the tissue fluids. The existence of tertiary calcium phosphate in the blood serum is doubted by many investigators since $Ca_3(PO_4)_2$ is not a known mineral and is unstable in water. Other investigators, particularly Gassman and Klement, maintain that calcium phosphate and carbonate exist in the body fluids as a complex or combined salt. Barille stated that calcium is found in the blood serum as unstable double salt, calcium carbonphosphate, which is soluble only at normal blood concentration of CO_2, and dissociates into its two neutral constituents, calcium phosphate and calcium carbonate, when the CO_2 content is reduced. Greenberg and Schmidt showed at the p_H of the body, the protein fraction of calcium in the serum is bound to casein in a complex nonionized form. It is generally accepted that the amount of calcium in the blood serum is greater than can be held by a salt solution of similar phosphate and carbonate content even after deducting the protein fraction. It is also agreed that the equilibrium of the solution of the calcium salts may be easily upset by disturbances in the concentration of calcium, phosphate, phosphatase, and CO_2 of the body fluids.

The Chemical Composition of Calcium Deposits.—Barr has pointed out that analytical studies of calcification reveal the presence of calcium phosphorus, carbonate, magnesium, small traces of alkaline salts, and occasionally traces of iron and silica. The two chief constituents of all calcium deposits are calcium phosphate and calcium carbonate. Howland and his associates found the ratio of residual calcium to residual phosphorus in fresh and old bone was 1:94, the ratio necessary for the formation of tertiary calcium phosphate $CO_3\ (PO_4)_2$. Kramer and Shear analyzed normal bone and pathological calcifications and found all the ratios averaged 1:96. Barr has shown that the constant presence of calcium phosphate and carbonate in all calcifications and the approximate constancy of their relative amounts has led to the assumption that these two salts are combined in definite proportion to form a compound or giant molecule, as hypothecated by Hoppe-Seyler, in 1877, and substantiated by the recent studies of Taylor and Sheard, Bogert, Hastings, and others.

Classification of Calcification of the Kidney.—The aforementioned classification of pathological calcification may be readily adapted to the different types of renal calcification. We have classified renal calcification into three distinct types, as follows:

I. Metastatic calcification of the kidney (*Kalkmetastasen*) which occurs in those various bone diseases accompanied by a hypercalcemia.

II. Non-metastatic calcification associated with a renal lesion which causes a decreased solubility of the calcium salts of the blood and tissue fluids or results in the faulty or impaired excretion of calcium salts from the kidney—the so-called *Kalkgicht* of Schmidt.

III. Non-metastatic (dystrophic) calcification associated with a renal lesion in which the precipitation of calcium salts occurs in tissues presenting degenerative, vascular, or retrogressive changes.

In Type I, the essential factor is an increase in the calcium salts of the blood which is due to the absorption of these salts from the bone lesions. The majority of these cases develop in the absence of a renal lesion.

In Type II, the important factor is a

renal lesion which may be primary (*i.e.*, acute or chronic nephritis, arteriosclerosis) or secondary (*i.e.*, toxic degenerative nephrosis). Hypercalcemia is not essential to this type of calcification although the degree of renal calcification is more marked in those cases accompanied by a transitory or permanent increase in the blood calcium.

In Type III, the essential factor is also a renal lesion which may be of an infectious, obstructive, traumatic, or neoplastic character. Hypercalcemia does not play a primary rôle in this type of calcification.

In this paper the authors will confine themselves to a discussion and presentation of cases based upon the following classification:

Calcification of the Kidney

I. Metastatic calcification — *Kalkmetastasen* (Type I).
   (*A*) Osteitis fibrosa cystica (hyperparathyroidism)
   (*B*) Osteomalacia, osteopsathyrosis, and osteitis deformans
   (*C*) Rickets and renal rickets
   (*D*) Osteosclerosis
   (*E*) Myeloma
   (*F*) Fractures
   (*G*) Lesion of the spinal cord
   (*H*) Primary osseous neoplasms and neoplastic osseous metastases

II. Non-metastatic calcification — *Kalkgicht* (Type II)—associated with an acute or chronic nephritis.
   (*A*) Acute or chronic nephritis
   (*B*) Nephrosis
   (*C*) Primary sclerosis (arteriosclerosis)
   (*D*) Experimental nephritis

III. Non-metastatic calcification of the dystrophic type, *i.e.*, destructive or degenerative lesions of the kidney (Type III).
   (*A*) Acute or chronic infectious lesions
      1. Acute or chronic pyelonephritis
      2. Abscess of the kidney
      3. Tuberculosis
      4. Bilharziosis
      5. Perinephritis or paranephritis
   (*B*) Obstructive or degenerative lesions
      1. Hydronephrosis
      2. Pyonephrosis
   (*C*) Tumors of the kidney
      1. Cystic lesions
         (*a*) Solitary cysts
         (*b*) Echinococcus cysts
         (*c*) Perirenal and peripelvic cysts
         (*d*) Polycystic diseases
         (*e*) Congenital cyst
         (*f*) Dermoid cyst
      2. Benign tumors
         (*a*) Fibroma and adenoma of the renal capsule
      3. Malignant tumors
         (*a*) Hypernephroma
         (*b*) Sarcoma
         (*c*) Mixed tumors
   (*D*) Vascular disease
      1. Arterial calcification
      2. Aneurysm of renal artery
   (*E*) Injuries of the kidney
      1. Intrarenal
      2. Extrarenal
         (*a*) Perirenal hematoma
         (*b*) Perirenal and pelvic cysts
         (*c*) Pseudohydronephrosis
   (*F*) Renal lithiasis
      1. Microlithiasis
      2. Cortical stones
      3. Putty-like bodies
      4. Sandy material

IV. Calcification of the kidney associated with gastro-intestinal diseases (Type II).
   (*A*) Pyloric obstruction
      1. Gastric or duodenal ulcer
      2. Gastric or duodenal carcinoma
   (*B*) Intestinal lesions
   (*C*) Cirrhosis of the liver
   (*D*) Dysentery
   (*E*) Undetermined gastro-intestinal diseases
   (*F*) Dietary deficiencies or faulty nutrition

V. Miscellaneous group (Type II).
   (*A*) Leukemia and other blood diseases
   (*B*) Senile type

Ossification of the Kidney—Osseous Metaplasia

   (*A*) Hydronephrosis or pyonephrosis
   (*B*) Renal calculi
   (*C*) Renal tumors
      1. Cysts—solitary and echinococcus
      2. Hypernephroma and sarcoma
      3. Mixed tumors
   (*D*) Vascular lesions
      1. Endothelioma
      2. Infarct

I. METASTATIC CALCIFICATION

Cases of metastatic calcification in the kidney associated with bone diseases have been reported by Virchow, Askanazy, Beer, Hofmeister, and Wells. The most common sites of metastatic calcification are the lungs, stomach, and kidney. The

predilection for these organs becomes more striking when one considers that calcification rarely occurs in these organs independent of a local lesion. In 1913, Hofmeister maintained that metastatic calcification occurred in those organs whose tissues possess a high alkalinity which is obtained by the continuous excretion of acids, *i.e.*, CO_2 in the lungs, HCl in the stomach, and orthophosphoric acid in the kidneys, thus leaving the tissue more alkaline. He also pointed out that calcium salts are less soluble in an alkaline than in an acid medium. Ordinarily, the amount of calcium in the blood is too slight to be precipitated, but when supersaturation of calcium salts occurs as a result of absorption of these salts from the skeleton, precipitation takes place in those organs where the alkalinity of the tissue fluids is greatest or the CO_2 concentration the least.

It is generally recognized that the principal factor influencing metastatic calcification is an increase in the calcium content of the blood, *i.e.*, hypercalcemia. This increase of calcium in the blood is the result of extensive destruction of the bone.

Various experiments have been undertaken to reproduce metastatic calcification. Tanaka (1911) and Katase (1913) showed that the intraperitoneal subcutaneous or intravenous injection of calcium salts, $Ca_3(PO_4)_2$, or Ca $(C_3H_5O_2)_2$, resulted in calcification of organs distant from the site of injection which had only a partial resemblance to the clinical metastatic calcification. Dixon and Hoyle, Kreitmar and Moll, Smith and Elvove, and others obtained calcification of the lungs, kidneys, and heart as a result of the hypercalcemia caused by the rapid decalcification of the bone following the administration of irradiated ergosterol. Metastatic calcification of the kidney has been observed following the administration of parathormone by Huepner (1927), Jaffe, Bodansky, and Blair (1931), and Moehlig, Murphy, and Reynolds (1935). Rabl observed typical metastatic calcification in his experimental studies by the alternate addition of acid or alkali to a high calcium diet.

(*A*) *Osteitis Fibrosa Cystica.*—Osteitis fibrosa cystica, often spoken of as "osteitis fibrosa," was first described by von Recklinghausen in 1891. The relationship of the bone changes in osteitis fibrosa cystica to parathyroid hyperplasia (adenoma) was emphasized by Barr, Bulger, and Dixon (1929), who called the clinical syndrome "hyperparathyroidism."

The presence of calcium metastases in osteitis fibrosa cystica was first reported by Askanazy (1903). Gaugele (1907) observed calcium deposits together with stones in the ureter and pelvis, causing hydronephrosis and pyelonephritis, in a female 37 years of age, dying of uremia. Other cases of calcium metastases in osteitis fibrosa cystica have been reported by Meyer (1917), Hoffheinz (1925), Parriera and Castro-Friere (1926), Penecke (1926), Akerberg (1927), Barr and Bulger (1930), Ask-Upmark (1931)—two cases, Berner (1931), Bergstrand (1931), and Noble (1932), Ettinger and Magendantz (1934), Albright and Bloomberg (1935), and MacCallum. The calcium metastases were accompanied by renal calculi in the cases reported by Hoffheinz, Parriera and Castro-Friere, Noble, Barr and Bulger.

In 1934, Albright, Baird, Cope, and Bloomberg reviewed the renal complications in 83 cases of hyperparathyroidism. They distinguished three distinct groups, *viz.:* (1) kidney disease, *i.e.*, pyelonephritis, secondary to the formation of calcium phosphate stones in the renal pelvis; (2) acute parathyroid poisoning with anuria and accompanied by calcium deposits in the kidney and other organs in the absence of chronic parenchymatous changes in the kidneys, and (3) an intermediate group in which the kidney disease (chronic glomerular or vascular nephritis) was due to calcium deposits which occurred in the kidney and not in the other organs. There were 21 cases in the first group, 17 in the third, and one in the second.

The pathology and pathogenesis of metastatic calcification of the kidney in osteitis fibrosa cystica (hyperparathyroidism) has been the subject of comprehensive

study by Albright and his associates, and in the following descriptions we have drawn extensively from their excellent contributions. It is well to point out that while their observations deal specifically with the calcium deposits in the kidney in hyperparathyroidism, these same observations may be extended and applied to metastatic calcification of the kidney in the other destructive diseases of bone.

The calcium deposits in the intrarenal urinary passages may appear as minute spheroidal or punctate areas or linear masses. The minute punctate areas resemble white flecks or dots which are faintly discernible on the cut surface of the cortical tissue and are often confused with small areas or fatty degenerations or with gas bubbles in the stellate veins. The linear masses appear as white streaks in the papillæ running parallel to the tubules. These papillary deposits usually make the pyramids stand out clearly but occasionally bear a close resemblance to uric acid infarcts, which can be easily distinguished by chemical tests. The small punctate masses are rarely seen on the surface of the kidney. Occasionally the calcium deposits in the pyramids may be very extensive and appear in the roentgenogram as wedge-shaped shadows conforming to the outline of the pyramids, as occurred in the cases reported by Akerberg, Ettinger and Magendantz, and Albright, Baird, Cope, and Bloomberg. It appears that the size and extent of these calcium deposits varies with the duration and severity of bone destruction, the degree of hypercalcemia with its resultant disturbance in the crystalloid-colloid equilibrium of the blood and urine, and the degree of renal impairment.

The microscopic examination usually reveals characteristic findings in these cases of metastatic calcification, *viz.:* precipitation of calcium salts in the epithelium of the tubules and formation of calcium casts in the lumen of the tubules. Calcium deposits are found less frequently in the interstitial tissues and walls of the blood vessels, including the glomerular loops and capsule. The presence of calcium in these deposits and casts is readily confirmed by using Von Kossa silver stain, which is specific for calcium salts and stains them black.

Albright and Bloomberg (1935) have stressed the intimate relation between the calcium deposits in the intrarenal urinary passages and the fine granular casts in urinary sediment of patients with hyperparathyroidism. These granular casts which are extremely fragile and composed chiefly of calcium phosphate, have the same appearance microscopically as amorphous phosphates and are similar in structure to the individual or conglomerate calcium casts found in the tubules in clinical and experimental hyperparathyroidism. They believed that the tubular casts are directly related to the formation of stones in hyperparathyroidism, and considered these casts as microscopic calculi in the tubules. In their opinion, the same factors, *i.e.*, concentration in the urine of calcium of phosphates and of hydrogen ions, govern the formation of these calcium casts as well as stone in hyperparathyroidism.

(*B*) *Osteomalacia, Osteopsathyrosis, and Osteitis Deformans.*—There are very few reports of metastatic calcification in these bone diseases, despite the fact that frequent reference is made of their calcification. As early as 1854, Steibel and, in 1875, Senator commented upon the occurrence of calcium deposits in the kidney in osteomalacia. Schonenberger (1901) reported calcium infarcts in the kidney in a case of osteomalacia complicated by multiple sarcomas and multiple fractures. Oppenheimer (1923) found calcium metastases in the kidney in two cases of osteoporosis (osteomalacia) in his series of 34 cases. Taterka and Denkin (1927) reported a case of renal calculi and calcium metastases in a woman 37 years old, who had suffered from rickets in childhood and later showed distinct osteomalacic traits.

Taterka and Denkin also reported a case of concrement formation and calcium metastases following osteopsathyrosis in

a man 41 years old who had also sustained six fractures. They considered the formation of calculi as calcium metastases in both cases, due to a disturbance of hormonal equilibrium, with a resultant disturbance of calcium metabolism.

We have recently described six cases of renal calculi in osteitis deformans, but unfortunately, were able to study the kidneys histologically only in one case showing numerous small stones and a severe pyelonephritis but no calcium deposits. We have been unable to find any case reports of calcium metastases in the kidney in this disease.

(*C*) *Rickets and Renal Rickets.*—There are relatively few references to occurrence of metastatic calcification in either of these diseases. Gierke (1902) and Schmorl (1904) mentioned the occurrence of calcium metastases in rickets. In 1907, Glaserfeld studied the incidence of metastatic calcification of the kidney in 70 autopsies on children and found calcium deposits in the kidneys of 10 of the 19 children with rickets. Reference has already been made to the interesting case reported by Taterka and Denkin. Chown (1936) reported a case of calcium deposits in the kidney of an infant who had had pyuria, bacilluria, and marked craniotabes. In 1936, Butler, Wilson, and Farber reported a case of late rickets in a 10-year-old boy who had diffuse calcification of the pyramids of both kidneys (confirmed by operation). An analysis of the calcified material showed a calcium carbonate phosphate compound of the same composition as bone. Albright, Dienes, and Sulkowitch observed a similar case.

In 1883, Lucas called attention to the association of chronic renal disease with marked deformities and alterations in the growth of bones in five cases. This syndrome has been designated as "renal rickets," whereas "renal dwarfism" is employed to denote the small stature and stunted growth that may accompany chronic interstitial nephritis in early life. In 1930, Mitchell pointed out that a disturbed relation between the calcium and phosphorus of the blood may exist in renal rickets, usually in the form of hypocalcemia, the reverse of the conditions in hyperparathyroidism. Mitchell observed a heavy amorphous deposit of calcium salts in the tubules and pelvis of each kidney in a case of renal rickets. Lightwood (1932) reported extensive calcium deposits in the kidneys of a female infant of seven months, a case of renal dwarfism associated with calcinosis and arterial calcification. Ellis (1935) observed also a case of calcium deposits associated with renal dwarfism in a six-year-old boy who had no complaint of urinary symptoms. Chown (1936) reported calcium deposits in the kidneys of two sisters who died in early infancy, suffering from severe congenital renal rickets. Asher noted calcification in the kidney in infantilism with bony changes resembling rickets.

It is generally assumed that renal disease, present in renal rickets, causes the bone lesions. However, Chown suggested that the reverse may be true, *viz.*: the hypercalcemia due to the bone disease causes the nephritic lesion. The renal disease usually manifests itself as a chronic interstitial nephritis (nephrosclerosis), with intratubular and peritubular calcium deposits which may be accompanied by varying degrees of acute or chronic pyelonephritis or congenital anomalies.

(*D*) *Osteosclerosis.*—This disease, also known as "Albers-Schönberg disease" and "marble bones," occurs most frequently in adults but is occasionally seen in children. The disease process is characterized by an excessive calcification of the bones, with an increased fragility and, in addition, there is found extensive metastatic calcification in the lungs, arteries, and tendons. The kidney may occasionally show metastatic calcification, as in the case reported by Schultze.

(*E*) *Myeloma.*—The occurrence of calcification in the kidney as well as in the gastric mucosa and alveolar walls of the lungs in a case of myeloma was first noted by Bender in 1902. Perla and Hutner (1935) studied the renal changes associated

with Bence-Jones proteinuria and multiple myeloma, and found 36 cases in the literature with description of kidney changes. They reported two personal cases with calcification of the tubules and collected eight similar cases. They maintained that there are three characteristic pathological changes in the kidney of multiple myeloma, no one of which is constant but all three may be present, *viz.*: (1) arteriosclerosis of the kidney, (2) nephrosis, (3) calcium deposits in the renal tubules. It seems highly probable that the injury to the tubules, caused by the nephrosis, predisposes to the deposition of calcium in the tubules.

(*F*) *Fractures.*—In a recent paper entitled "Urinary Calculi in Bone Diseases," we studied the development of renal calculi following fractures of the bony pelvis and long bones. At that time it was apparent that a variety of local and constitutional changes may accompany or follow any fracture and serve as predisposing factors in the formation of renal calculi and calcium deposits in the kidney. While the explanation of the latter phenomenon is not always available, a causative relation may be assumed in the presence of the following conditions: (*a*) renal lesion antedating the fracture or occurring at the time of injury or originating through complicating infections; (*b*) temporary or permanent disturbance in the crystalloid-colloid balance in the blood and urine which may be due to decalcification of injured bone, prolonged immobilization, infection of the injured bone, delayed or poor healing, etc.

Reports of metastatic calcification associated with fractures are rare. Akerberg (1932) reviewed the subject and found relatively few cases, due possibly to the reluctance or disinterest on the part of urologists and pathologists to report isolated cases.

(*G*) *Lesions of the Spinal Cord.*—Myer has reported metastatic calcification of the kidney and dystrophic calcification and ossification of the muscles of the lower extremities following transverse lesions of the spinal cord. He attributed the calcium deposits in the kidney in these conditions to withdrawal of calcium from the paralyzed extremities and to the calcium content of the blood. He maintained that the calcium was transported chiefly by the lymphatic vessels as seen in roentgenograms of fractures, articular tuberculosis, and Gritti's amputations. Undoubtedly, the presence of an ascending cystopyelitis resulting from the bladder paralysis, with its attending stasis and infection, plays some rôle in the development of metastatic renal calcification. The secretory function of the kidney is impaired as a result of these infectious changes, and the increased alkalinity of the renal tissue caused by the elimination of acids favors the precipitation of calcium salts which are present in the blood and tissues in an excessive amount.

(*H*) *Primary Osseous Neoplasms and Neoplastic Osseous Metastases.*—Primary osseous neoplasms and osseous metastases from a carcimona or sarcoma may produce extensive destructive lesions in the bones, with subsequent disturbances in the calcium metabolism. These latter changes predispose to the formation of calcium deposits in various organs in the body, particularly in the presence of an accompanying nephritis. Metastatic calcification is observed more frequently in cases of secondary osseous metastases from a carcinoma (Verse, Hastings *et al.*, Klotz, Harris) or sarcoma (Litten, Lazarus and Daresdau, Stade, and Askanazy) than in primary neoplastic diseases of the bone. In many of these cases the metastatic calcification may be extensive but rarely involves the kidneys. Adamson, Boyd, and Cameron observed a case of extensive calcium deposits in the kidney due to destruction of the bone by metastatic bronchogenic carcinoma in an 18-year-old male.

II. NON-METASTATIC CALCIFICATION

(*Calcification Associated with Acute or Chronic Inflammatory Diseases of the Kidney* (*Kalkgicht*), *Type II*)

(*A*) *Acute or Chronic Nephritis.*—For many years following Virchow's original

description of calcium deposits in the kidney it was believed that these changes were always associated with bone disease. In 1904, Beer collected records of 12 cases associated with bone disease and 22 cases unassociated. Beer reviewed 100 autopsies and found 53 cases of calcium deposits in the kidney associated with various diseases, among which was chronic nephritis. He pointed out that calcium deposits were found only in diseased kidneys and stressed the influence of local changes in the kidney, either nutritional or toxic in origin, upon the deposition of calcium salts.

As early as 1882, Kidd reported extensive calcium deposits in the kidneys of two males, aged 34 and 30 years, respectively, who had chronic renal disease. In 1899, Brill and Libman described a case of calcification of the kidney, associated with calcification in the liver, in a 14-year-old girl who died of chronic interstitial nephritis. In 1920, Schmidt maintained that the decrease of albumin in the blood, which occurred as a result of increased elimination through the chronic nephritic kidney, altered the solubility of the calcium salts in the blood and influenced the deposition of these salts in the kidney. He described the presence of fine granular deposits of calcium salts in the interstitial tissue and tunica propria of the tubules, following hyaline degeneration in the kidney of senile individuals.

Recent clinical investigations by Greenwald, Nelkin and Steinmetz, and others have disclosed a marked disturbance in calcium and phosphorus metabolism in the various affections of the kidney. The most notable changes in the calcium and phosphorus content of the blood in chronic nephritis are: (*a*) an appreciable lowering of the serum calcium and an elevation of inorganic phosphates, and (*b*) the serum calcium is inversely proportional to the amount of urea and inorganic phosphates.

Weiss (1922) reported a case of chronic nephritis accompanied by extensive tubular deposits of calcium in both kidneys and nephrolithiasis in one of the kidneys of a 14-year-old girl. Bergstrand (1923) described a case of renal insufficiency with cortical atrophy (chronic glomerular nephritis) caused by heavy deposits of calcium in the papillæ. In this case he also observed small cystic degenerative areas in the papillæ containing minute calcareous particles. Several of these cystic areas communicated with the pelvis and were responsible for the presence of loose calcareous particles in the pelvis.

(*B*) *Nephrosis.*—In 1930, Patrassi made a comprehensive review of the subject of calcification in Bright's disease, reporting his observations in 41 cases of calcium deposits in a series of 483 cases with renal disease. He found calcium deposits in 18 of 43 cases of tubular nephritis, in one of 10 cases of acute and subacute glomerulonephritis, in eight of 17 cases of chronic glomerulonephritis with secondary sclerosis, in 14 of 58 cases of primary renal sclerosis, and none in 20 cases of renal affections other than Bright's disease, *i.e.*, renal tuberculosis, acute pyelonephritis, etc.

(*C*) *Primary Sclerosis* (*Arteriosclerosis*).—Kitt (1895) was the first to describe the presence of heavy deposits of calcium in the cortex of primary sclerotic kidneys. Baum (1900) observed calcification of the glomeruli in senile atrophic kidneys due to arteriosclerosis. The incidence of such changes is greater than formerly supposed, a fact substantiated by Patrassi's findings. The calcium deposits are found in the tubules and glomeruli. This type of cortical calcification belongs to the dystrophic group and is due to the deposition of calcium in the various component structures in the renal cortex which present retrogressive changes, *i.e.*, hyalinization, fibrosis, degeneration resulting from the primary vascular sclerosis.

(*D*) *Experimental Nephritis.*—Calcium deposits in the kidney have been produced experimentally by general intoxication with the following substances: (1) aloes (Gottschalk, Neuberger); (2) bichloride of mercury (Virchow, Schmidt, Verse and others); (3) bismuth subnitrate (Langhans,

Neuberger); (4) carbolic acid (Schinchiyo-Uyeno); (5) chronic acid (potassium chromate) (Neuberger); (6) copper sulphate, iodine, and iodoform (Von Kossa); (7) glycerin, pyrogallic acid, arsenic, and veratrin (Afanassiew); (8) lead acetate (Prevost and Binet); (9) naphthol (Schmidt); (10) oxalic acid and potassium oxalate (Franklen, Neuberger and others); (11) phosphorus (Neuberger), and (12) tuberculin of Koch (Docray). Similar changes have been observed experimentally following the injection of the following chemicals directly into the kidney substance: (1) formalin (Putti); (2) bichloride of mercury (Tartarini-Gallerani), and (3) lysol, phenol (ortho-, meta-, or para-cresol) (Bolognesi).

As a general rule, the calcium infarcts, which develop following the intravenous injection of these various chemicals, appear as fine granulations in the tubules of the cortical zone, occasionally in the medullary, area, and rarely in the glomeruli. They may be found in the walls, epithelium, and lumen of the tubules or in the surrounding interstitial tissue. In the lumen of the tubules, they conform to the shape of the lumen and appear black to transparent light and white to reflected light.

III. NON-METASTATIC CALCIFICATION OF THE DYSTROPHIC TYPE

(Calcification Associated with Destructive or Degenerative Lesions of the Kidney, Type III)

(A) Acute or Chronic Infectious Lesions

1. Pyelonephritis.—Newman was one of the earliest writers to emphasize the occurrence of calcified inflammatory products in the kidney. Baetjer (1907) pointed out that suspicious shadows simulating those of renal calculi may be caused by dense cicatrices of the kidney. In a discussion of the chronic form of hematogenous nephritis of bacterial origin and the interesting sequelæ of this condition, W. J. Mayo (1919) mentioned the occasional deposits of calcium carbonate in an area which is usually situated close to or connected with the capsule and produces a shadow on the roentgenogram closely resembling that of a renal calculus. Albright, Dienes, and Sulkowitch reported two cases of diffuse calcification of the pyramids of both kidneys secondary to a chronic pyelonephritis caused by the *Hæmophilus* influenza, a small gram-negative bacillus with urea-splitting properties. In both cases, sulfanilamide therapy promptly eliminated the organisms from the urine.

2. Abscess of Kidney.—Mathe presented a roentgenogram showing a calcified area in the lower pole of both kidneys. These shadows represented calcification of a cortical abscess of the subacute or chronic urogenous type resulting from stasis of the urinary tract.

Case I (G. U. 3,000), W. P., male, 30 years of age, married, clerk, was referred by his family physician on Sept. 25, 1925, because of pus in his urine. His chief complaints were a tired feeling and pain in the right lumbar region and right hip. There was no history or symptoms of genito-urinary disease. At this time, physical examination was essentially negative and urinalysis disclosed no abnormal findings. Cystoscopic and pyelographic studies revealed no evidences of disease in the kidney, ureter, or bladder. Despite the absence of any infection, it was felt that we were dealing with an intermittent type of pyelonephritis, and further observation and re-examination were advised. Subsequent study revealed a bilateral staphylococcal pyelonephritis and chronic prostatitis due to the same organism. Treatment directed toward eradication of these infections was instituted with relatively little improvement. The infectious process in the left kidney proved very resistant to all internal medication and instrumental treatment, and the kidney underwent pyonephrotic changes which were confirmed by pyelographic study on Sept. 2, 1926. At this time, no evidence of calculi or calcification were detected on the roentgenogram or pyelogram.

On Nov. 12, 1926, the kidney was removed and the patient made an unevent-

ful recovery. Following the operation, the patient returned for regular and periodic treatment of his prostatic and right renal infections, which have been completely eradicated.

The operative specimen revealed the surface changes of a chronic pyelonephritis including several small cortical cysts. On cross-section, an abscess 8 mm. in diameter was found in the medullary area in the central portion of the kidney. The abscess contained thick pus and minute calcareous fragments. When these were washed away, calcareous particles were found lining the walls of the abscess cavity.

3. Tuberculosis.—The deposition of calcium salts in tuberculous lesions of the kidney is considered a part of the pathological process of this disease and is a relatively common finding. From a pathological standpoint, the nature of the calcium deposits varies in the different types of renal tuberculosis and for practical purposes may be classified under two general headings: (*a*) the deposition of calcium salts in solitary or multiple ulcerative lesions situated at or near the tips of the pyramids, and (*b*) calcification of single or multiple caseated areas in the parenchyma with or without involvement of the renal pelvis and ureter.

The pathological significance of calcification in the renal tuberculous lesions has been the subject of much conjecture. Some investigators consider calcification as representing a stage of healing, while others believe it is part of the general repair process. The latter view appears to be more logical and conforms with the general pathological concept that any dead or damaged tissue, so large that it cannot be readily absorbed, may become infiltrated with calcium salts. In a similar manner the deposition of calcium salts in the caseated and necrotic tissue of tuberculous lesions may be interpreted as an attempt to wall off the infectious process. The calcium salts are obtained from the circulation and are not the result of specific cell differentiation (metaplasia). That calcification of a renal tuberculous lesion is not genuine evidence of healing is corroborated by the fact that active tubercle bacilli may be found within completely calcified areas.

The incidence of calcification in renal tuberculosis is relatively high. Unfortunately, accurate histological studies on calcification in renal tuberculosis are not available but undoubtedly would yield an even greater incidence than the following roentgenographic statistical studies.

Caulk (1915) reported some degree of calcification in 20 per cent of the cases of renal tuberculosis. Braasch and Olsen (1919) reported that pre-operative roentgenographic studies were made in each of the 131 patients operated upon for renal tuberculosis at the Mayo Clinic in 1916 and 1917, and positive shadows suggestive of renal tuberculosis were present in 30 cases (22 per cent). Stevens (1926) found typical shadows due to tuberculous calcification in seven of 15 consecutive cases in which roentgenograms were taken. Crenshaw reviewed 1,817 cases of renal tuberculosis at the Mayo Clinic from 1910 to 1928 and found 131 cases (7.1 per cent) with calcification. The incidence of calcification is even greater in cases of occluded renal tuberculosis, as evidenced by the fact that Crenshaw found calcification in 30 per cent of the occluded type in the series of 1,817 cases. The greater incidence of calcification in the occluded type of renal tuberculosis is attributed by Braasch to the fact that such lesions are of longer duration and hence have more opportunity for calcification.

Gibson has pointed out calcification is even more frequent in cases of true autonephrectomy, *i.e.*, asymptomatic cases with occlusion of the ureter with total destruction and transformation of the kidney into a calcified mass. Crenshaw found total calcification in 10 cases (0.5 per cent) in the series of 1,817 cases. The duration of illness in cases showing complete calcification of the kidney is striking. Birkelo reported a case in which the primary illness dated back 43 years. In Gibson's

patient, the disease process had been present for 35 years, and in Conybeare's patient 25 years. Dewitt reported a case of clinically healed tuberculosis of 15 years' duration in which he found three calcified areas in the kidney. Scholl observed a case of total calcification of six years' duration in a nine-year-old child.

The types of shadows seen in the roentgenogram in renal tuberculosis have been classified by Braasch and Olsen, Eisendrath, Stevens, and others under three general headings in order of their frequency:

Group I. Scattered small areas in the form of single elongated streaks or multiple punctate areas which are usually confined to one pole of the kidney.

Group II. Single or multiple isolated and circumscribed areas which are of irregular outline and variable density.

Group III. Large irregular shadows of variable density involving a large portion of the entire kidney.

Groups I and III are sufficiently distinct and characteristic to be considered pathognomonic of renal tuberculosis. In the first group, the calcification is a more or less localized process but is not a true indication of the degree of tuberculous infection present. It is well recognized that calcification rarely, if ever, occurs in the early stages of renal tuberculosis and, furthermore, that extensive tuberculous destruction may occur without any demonstrable signs in the plain roentgenogram or pyelogram, due to the fact that the pelvis and calices are not involved and the tuberculous areas have the consistency and density of normal tissue. These areas cast a shadow only when calcium is deposited in the caseated or necrotic areas. The intensity of the shadows may vary in the same or different lesions. In some instances of early calcification, it is extremely difficult to detect the presence of pathologic shadows which may be very dim or scarcely discernible. In other cases, the involved areas are clearly delineated.

In Group II, the calcified shadows indicate a more advanced stage of ulcerative renal tuberculosis. These shadows may cause difficulties in differential diagnosis as they are frequently confused with renal calculi. Their multiplicity, irregularity, and location in widely separated points in the parenchyma tend to differentiate these calcified tuberculous shadows from renal calculi. The shadows of tuberculous calcification are not as sharply defined as those of stones; the borders are relatively indistinct and gradually fade off into the surrounding tissue. However, it must be borne in mind that calculi may occur in a tuberculous kidney.

The third group includes the more advanced types of renal tuberculosis, *viz.:* the symptomatic occluded type and the asymptomatic autonephrectomized kidney. In these cases intravenous pyelography is useless because of the extensive destruction of renal tissue, and a retrograde pyelogram is often impossible because of advanced bladder changes or occlusion of the ureter. Consequently, the diagnosis is made from the plain roentgenogram. The kidney outline is usually smaller due to shrinkage and atrophy and lobulated with a marked thinning of the parenchyma due to the calcified masses. The calcified shadows in the kidney area are usually hemispherical or clover-leaf in outline. These cases are frequently referred to as a "putty" or "cement" kidney in the English literature, as "mortelniere" or "kittniere" by Germans, and as "rien mastic" by the French and Spanish. Calcification of the pelvic and ureteral wall (so-called canal tuberculosis) may be observed in the same cases.

Case II (G. U. 5,437), J. E., male, 30 years of age, married, clerk, was seen for the first time on Aug. 23, 1934. A left nephrectomy for renal tuberculosis had been performed in March, 1927, at another hospital. The patient was in apparent good health until January, 1931, when he developed urgency, frequency, burning, and dysuria which have persisted to date. Physical examination was essentially negative. Urine showed faint trace of albumin

and many pus cells and red blood cells. Stained smear of urinary sediment was negative for tubercle bacilli, but guinea pig inoculation was positive. Cystoscopic examination was essentially negative except for congested right ureteral orifice. Plain roentgenogram showed several irregular areas of calcification within the right kidney outline. A ureteropyelogram showed a normal pelvis but the terminal calices were irregular and moth-eaten in appearance (Fig. 1). The areas of calcification appeared to involve the pyramids of the kidney. The patient was treated with usual palliative measures.

Case III (G. U. 4,708), E. H. K., female, 48 years of age, married, was admitted to Sinai Hospital on May 18, 1935, complaining of pain in the right loin. Onset of present illness dated back three years, when she developed discomfort in the bladder region and had frequency of urination. She was examined by another physician who found pus in her urine. She complained of dull pain localized to the right lumbar region and right loin, which recurred at frequent intervals. Six weeks before she had had her first cystoscopic examination by another urologist, who found the pus coming from the right kidney. Intravenous urography failed to reveal any dye in the right kidney and no abnormal shadows were noted in the kidney. There was no history of renal colic or hematuria. Physical examination disclosed slight tenderness in the right upper and lower quadrants. A catheterized specimen of urine showed 15 to 20 pus cells and an occasional red blood cell. A stained smear showed several tubercle bacilli and many *B. coli*.

Cystoscopy and pyelography were performed on the above date. The pus was found to be coming from the right kidney. A guinea pig inoculation was made with the urine which was later reported positive. Plain roentgenogram revealed several irregular calcified shadows in the right kidney region. The right pyelogram showed the pelvis to be slightly dilated and the ends of the lower and middle calices were irregular and fuzzy in outline. The calcified shadows noted on the plain plate were found to extend outward from the tips of the calices and were considered to be evidences of calcification in old healing tuberculous abscesses (Fig. 2). Nephrectomy was performed and the patient made an uneventful recovery.

Case IV (G. U. 5,823), H. R., male, 31 years of age, married, was admitted to Sinai Hospital on March 12, 1936, complaining of pain on urination. The patient had always enjoyed good health except for cervical adenitis in 1921. For the past two years, he has noticed a urethral discharge due to a urethral stricture; he has been treated with dilatation with good results. In May, 1935, he had an attack of right renal colic and, following this, he had marked frequency, burning, and tenesmus. A tentative diagnosis of renal and vesical tuberculosis was made in February, 1936, and the patient received four injections of Koch's tuberculin. The urinary trouble has persisted to date. Physical examination was essentially negative except for several hard irregular nodules in both lobes of the prostate and in the right seminal vesicle. A voided specimen of urine gives a positive test for albumin and microscopically shows many pus cells and red blood cells. A stained smear shows numerous tubercle bacilli. Plain roentgenogram showed several calcified shadows in the right kidney region; also, there were several calcified shadows in the spleen and one irregular calcified shadow in the region of the right adrenal (Fig. 3).

Cystoscopy revealed extensive involvement of the right kidney and the bladder around the right ureter. There was a marked decrease in function in the right kidney. On March 24, 1936, a right nephro-ureterectomy was performed. The patient developed a post-operative atelectasis of the right lung; it cleared up promptly, and he was discharged from the hospital on April 23, 1936.

The right kidney was very large and soft throughout on the posterior surface; there was a small hemorrhagic cyst, and several

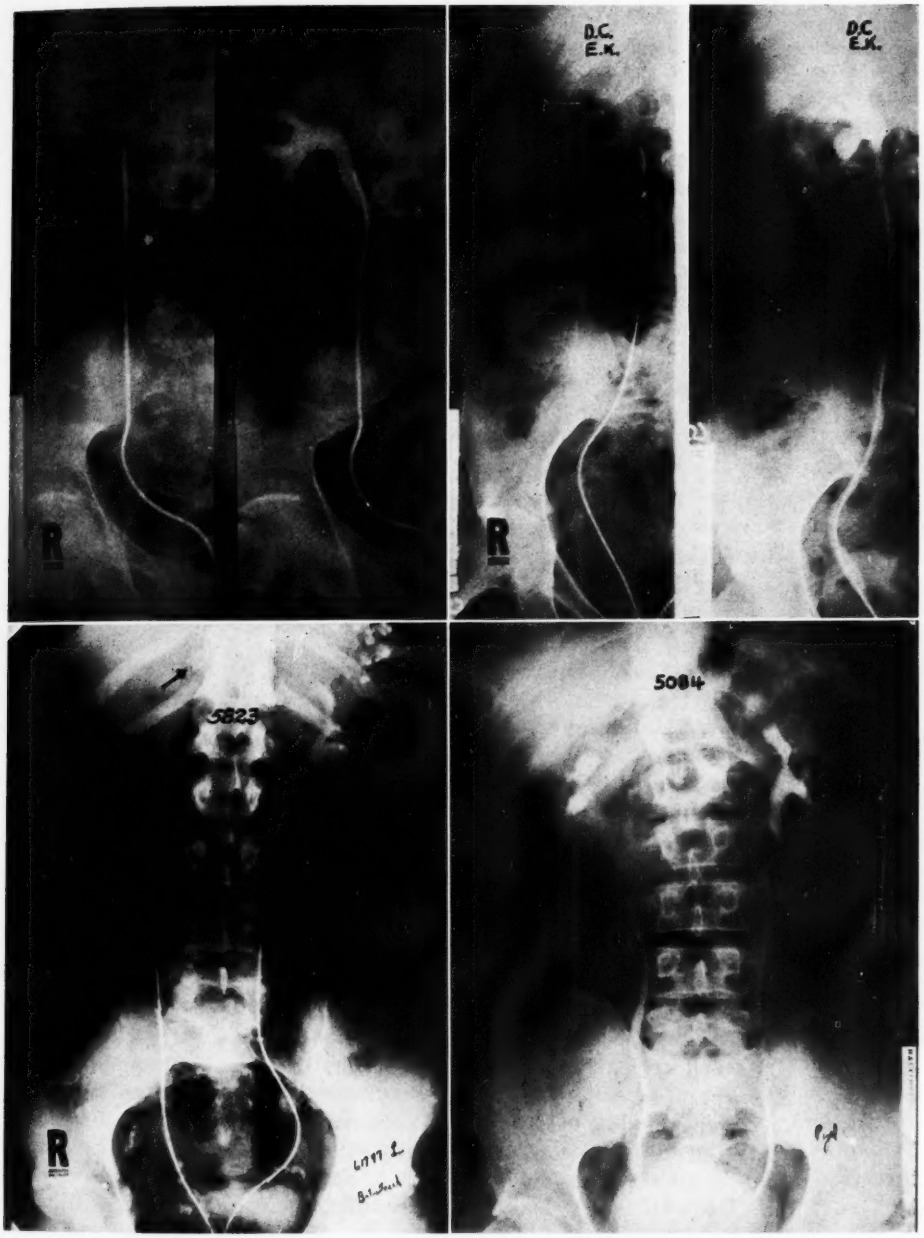

Fig. 1 (*upper left*). Case II. In the plain roentgenogram the arrows point to several irregular calcified shadows scattered throughout the parenchyma. In the pyelogram these appear to involve the pyramids and are interpreted as evidences of healing in old tuberculous abscesses. The moth-eaten appearance of the terminal calices is characteristic of tuberculosis.

Fig. 2 (*upper right*). Case III. The irregular calcified shadows in the plain roentgenogram are indicated by arrows. They appear to extend outward from the tips of the calices in the pyelogram.

Fig. 3 (*lower left*). Case IV. A bilateral pyelogram showing calcification of the right adrenal gland (indicated by the arrow), the spleen, both seminal vesicles, and the prostate.

Fig. 4 (*lower right*). Case V. A bilateral pyelogram showing the irregular fuzzy outline of the lower major calyx characteristic of tuberculosis. The calcified shadows appear to be in the parenchyma.

small abscesses in the upper portion of the kidney which showed a more extensive involvement than the lower pole. On cross-section there was found an extensive ulcerative and caseative tuberculous process in the upper pole of the kidney. These large abscesses contained a thick greenish pus in which some calcareous material was observed and in the walls of the abscessed cavities. Histological study revealed typical changes of renal tuberculosis.

The diagnosis in this case was (1) renal tuberculosis, right, with calcification; (2) tuberculosis of both seminal vesicles, both vas deferens and the prostate, with calcification; (3) tuberculosis of the spleen, with calcification; (4) tuberculosis of the right adrenal gland, with calcification.

Case V (G. U. 5,084), B. J. R., male, 36 years of age, married, merchant, presented himself for examination on Jan. 23, 1933, with a complaint of hematuria. He had always enjoyed good health until five weeks before, when he noticed blood in his urine. He called an urologist who made a diagnosis of renal tuberculosis. For the past five weeks he had been complaining of diurnal frequency, burning, and urgency. Physical examination was negative. Voided specimen of urine showed many pus cells and a few red blood cells. On Jan. 24, 1933, cystoscopy and pyelography were performed, and a diagnosis of right renal tuberculosis was made. A plain roentgenogram showed several small calcified shadows in the region of the right kidney. A right pyelogram showed the right pelvis and upper major calyx to be normal. The terminal portions of the middle and lower major calices appeared to be compressed and had irregular fuzzy outlines. The calcified shadows appeared to be in the parenchyma beyond the terminal portion of the lower major calyx (Fig. 4). On Feb. 7, 1933, a right nephrectomy was performed. The patient was discharged from the hospital on Feb. 21, 1933.

The operative specimen showed the kidney to be normal with small tubercles on the anterior and posterior surfaces of the lower pole. On cross-section, there were several small ulcerated abscessed areas extending from the tips of the pyramids to the parenchyma. The abscesses contained numerous minute calcareous particles which imparted a gritty sensation under the knife. Microscopic studies showed typical findings of tuberculosis with calcification.

Case VI (G. U. 3,808), G. W., aged 13 years, male, schoolboy, was referred for examination in 1928 because of pyuria. Following an attack of scarlet fever at the age of seven, his mother noticed that his urine was cloudy and occasionally contained large shreds of pus-like material. Two years later, he developed whooping cough and also showed pus in his urine. The patient did not complain of any pain or difficulty on urination, but frequently wet his bed at night. On May 12, 1928, he complained of pain localized to the right ureteral quadrant which did not radiate and lasted but ten minutes, being accompanied by nausea and vomiting. The pain recurred at frequent intervals during the following two days. Physical examination was entirely negative. A voided specimen of urine showed 50 to 60 pus cells per h.p.f.

Cystoscopy and pyelography were performed on June 18, 1928, and a diagnosis of right renal tuberculosis was made. The plain roentgenogram showed an irregular, large calcified shadow in the region of the right kidney, rather blotchy and simulating a bunch of grapes (Fig. 5). The diagnosis of a right renal tuberculosis of occluded calcified type was made.

On July 6, 1928, a right nephrectomy was performed. The patient made an uneventful recovery and was discharged from the hospital on July 26, 1928. The operative specimen showed an irregular nodular mass which had a brownish color in some areas and pinkish in others. Some of the nodular areas were soft and others were firm. On cross-section, a thick yellowish-gray pus exuded. The entire kidney was replaced by large cavities filled

with putty-like calcareous material; no evidences of any cortical medullary renal tissues were found.

4. Bilharziosis.—This is an extremely rare type of renal calcification. Lotsy described a case of bilharzia of the renal pelvis and the ureter which showed a round shadow with a darker border and two parallel linear shadows running downward from the pelvis toward the ureter on the roentgenogram. The shadows were due to calcium deposits originating in calcification of the numerous eggs of the parasite which, in the older cases, occupied all the layers of the wall of the bladder and ureter and, occasionally, the renal pelvis and the immediately surrounding tissues. Calcified demarcations of the bladder and ureters in cases of long standing bilharziosis have also been observed by Harlow and Afifi, Diamantis, and Afifi.

5. Perinephritis or Paranephritis.—Inflammatory changes may develop in the renal capsule following an acute or chronic pyelonephritis, perinephritis, or paranephritis. These changes are usually manifested in the form of a marked thickening or fibrosis of the capsule which may undergo hyalinization or impregnation with organic or inorganic salts. Perussia described a case in which partial calcification of the renal capsule was diagnosed as a stone in the kidney. Baetjer and Smart have called attention to the presence of calcium deposits in the scars in cortical areas of kidney following chronic suppurative diseases of the kidney. Mayo and Mathe have emphasized the presence of calcium deposits in cortical abscesses which are situated near or involving the capsule and are a sequel to chronic pyelonephritis.

Calcification of the perinephritic or paranephritic tissue secondary to an acute or chronic inflammatory process is rarely observed. However, Mathe, Wesson, O'Connor, and others have pointed out that distinctly abnormal shadows in the kidney region may be produced in the roentgenogram by inflammatory processes and are due to sclerosis or fibrosis of these tissues and their effect upon the kidney outline. Koll observed such shadows in cases of paranephritic abscess and stressed their diagnostic significance together with a careful history. Rosving has described four cases of sclerosing fibrous perinephritis in patients with uric acid diathesis. These capsular changes as a rule do not produce a shadow on the roentgenogram, although Illyes observed one case in his series of three which showed three irregular shadows in the kidney region.

(B) Obstructive or Degenerative Lesions

1. Hydronephrosis.—The presence of calcium deposits in hydronephrosis and pyonephrosis is rarely encountered. The earliest reference to this phenomenon was made by Rayer, in 1843, who described a specimen sent to him by Dr. Elliotson, of England, in 1834, for examination. The specimen was an atrophied kidney containing two shell-like formations formed by the dilated pelvis and the fibrous capsule. Rayer also cited a case of Jacques Sachs who found both kidneys transformed into a mass the consistency of alabaster in a female who had suffered from renal colic for several years. The description of the autopsy findings is very suggestive of a calcified pyonephrosis.

2. Pyonephrosis.—In his discussion of pyonephrosis, Roberts stated that the pus is gradually inspissated and impregnated with the carbonates and phosphates of lime and magnesia until the kidney is converted into a putty- or chalk-like material which fills up the compartments of the sacculated kidney. He also noted that occasionally the fibrous septa which separate the compartments are extensively calcified. Dickinson stated that the kidney may be practically destroyed by pyelitis and the products shut up in the pelvis until at last nothing remains but an innocuous, though useless, cyst containing a mass of chalky or mortar-like substance. He described a specimen in the museum of St. Bartholomew's Hospital obtained from a female, 62 years of age, and which was obviously a case of calcified hydrone-

phrosis. Very little of the kidney remained excepting a shell of fibrous tissue which was impregnated with a mortar-like substance composed of carbonates and phosphate of lime. Morris (1885) stated that calculous material is often deposited upon the lining of the cavities of the pyonephrotic kidney. McNaughton (1901) reported a case of right calculous pyonephrosis in a female which showed calcareous degeneration in the substance of the organ and calcium deposits lining the dilated calices. Baetjer (1907) stated that a purulent exudate in the renal pelvis, when inspissated and containing deposits of calcium, may cast a shadow indistinguishable from that of a renal calculus. He cited an unusual case in which a roentgenographic diagnosis of renal calculus (3 cm. in diameter) was made, and, at operation, the pus was found to be encapsulated by fibrinous tissue lined with a thin layer of calcium salts. Cases of calcification of hydronephrotic or pyonephrotic kidney have been reported by Goldenberg (1910), Groeschel (1912), Bauer (1913), Knerr (1918), and Arena (1920).

In a monograph on hydro- and pyonephrosis published in 1926, Hinman pointed out that not infrequently on cross-section of pyonephrotic kidneys, a thin pus escapes from the purulent cavities, leaving empty pouches and a dry semi-caseous material in which partial calcification exists. He also emphasized the fact that there may be considerable calcareous changes in such a dead kidney and, as atrophic changes progress, the calcified areas may be somewhat absorbed. A case of total calcification of the right kidney was reported by Wheeler in 1930. The condition was presumably a calcified pyonephrosis, as the patient gave no history suggestive of tuberculosis nor were any evidences of tuberculosis found on inoculation.

Case VII (G. U. 3,229), A. N., male, 61 years of age, married, tailor, was first seen on Aug. 3, 1936, complaining of pain in the left side of the abdomen. For the past two weeks he had been having frequent chills, accompanied by a dull pain in the left upper quadrant. The urine gave positive test for albumin and microscopically contained many pus cells and staphylococci. The plain roentgenogram revealed a large irregular calcified shadow in the center of the enlarged right kidney, with several shadows of lesser density in the lower pole (Fig. 6). The pyelogram showed a very large multilocular pyonephrotic kidney with calcareous deposits within the abscess cavities (Fig. 7). On Aug. 27, 1926, a left nephrectomy was performed under gas anesthesia. The operative specimen showed a very large pyonephrotic kidney with numerous abscess cavities containing a thick inspissated greenish pus in which calcareous material was found. The walls of these abscess cavities were also lined with calcareous fragments. Microscopic study of the tissue surrounding these cavities showed marked chronic inflammatory and fibrotic changes, with heavy round-cell infiltration and deposition of calcium salts.

Case VIII (G. U. 5,382), E. L., female, 48 years of age, married, housewife, was referred for examination on June 18, 1934. Her chief complaint was backache of seven years' duration. For the past year she had been troubled with a dull pain in the lower sacral and right lumbar region which occasionally radiated to the right upper quadratn. She has also been troubled with urgency, diurnal and nocturnal frequency, and burning, but no hematuria. Physical examination revealed tenderness in the upper and lower quadrants and lumbar regions on the right. Urine contained many pus cells.

Cystoscopy and pyelography disclosed a calculous pyonephrosis on the right. The plain roentgenogram showed a large calcified shadow occupying the pelvis and the upper and middle major calices (Fig. 8). In the lower pole of the kidney, there appeared to be several small shadows in the cortical area. On June 26, 1934, a right nephrectomy was performed, following which the patient made an uneventful recovery.

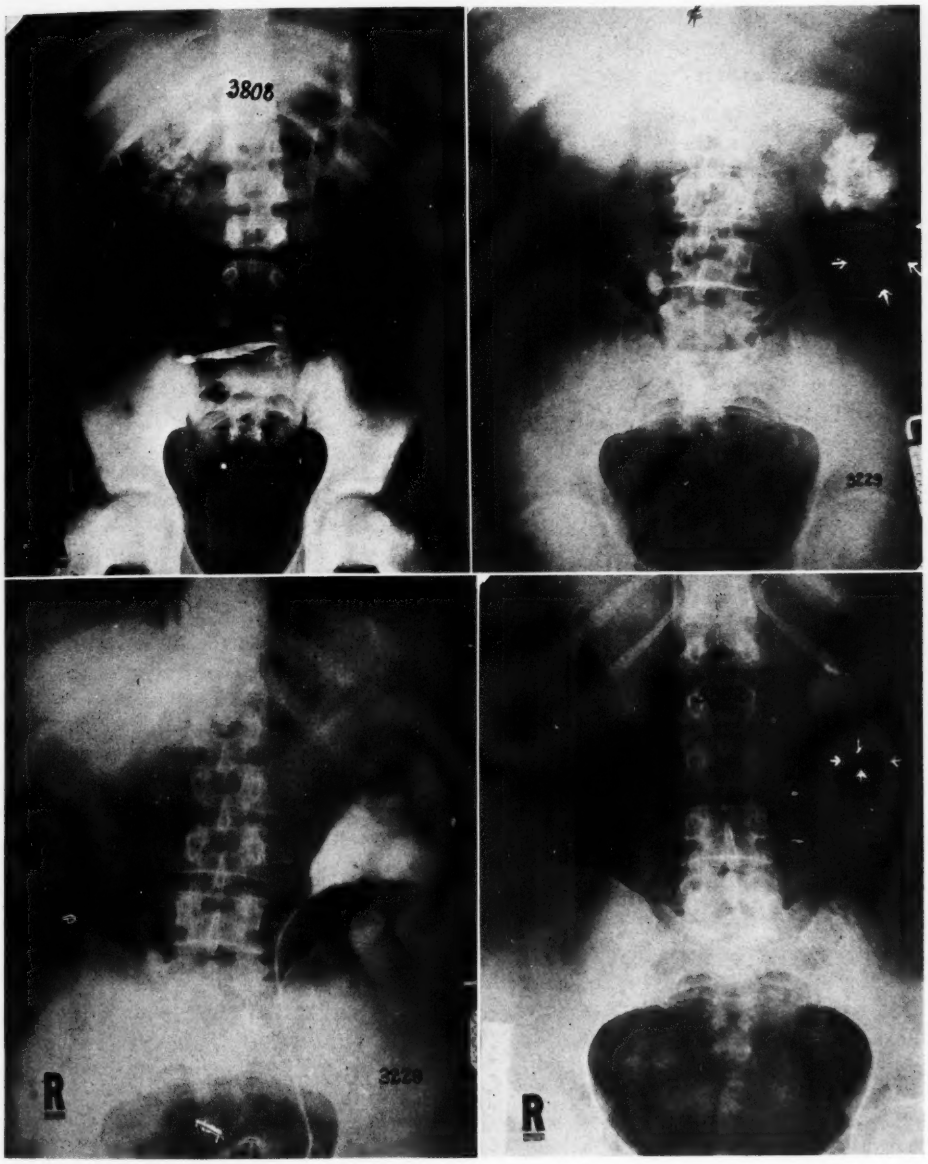

Fig. 5 (*upper left*). Case VI. A plain roentgenogram showing an irregular, large, calcified shadow in the right kidney area simulating a bunch of grapes and characteristic of the occluded calcified type of renal tuberculosis.

Fig. 6 (*upper right*). Case VII. A plain roentgenogram showing a large calcified shadow in the region of the pelvis and several irregular calcified areas of lesser density in the lower pole of the kidney (arrows). These shadows were interpreted by some observers as calculi but their blotchy appearance, irregular outline, and decreased density are more characteristic of calcium deposits in the walls of abscess cavities.

Fig. 7 (*lower left*). Case VII. A pyelogram showing a large multilocular pyonephrotic kidney. On comparing this film with the previous one (Fig. 6), it is apparent that the large dense shadow was confined to the pelvis and middle calyx, whereas the irregular shadows of lesser density corresponded to the lower major calyx. The operative specimen disclosed calcareous deposits lining the abscess cavities, but no calculi.

Fig. 8 (*lower right*). Case VIII. Plain roentgenogram showing a large calculus occupying the pelvis and upper and middle calices. The arrows point to several small irregular shadows of lesser density which are present in the cortical area of the lower pole.

The operative specimen revealed a large coral calculus, brownish-black in color, occupying the pelvis and upper and middle calices. The lower major calyx was markedly dilated and contained thick greenish pus. When this was washed away, yellowish-brown calcareous material was found lining the abscess cavity. A stricture which was present at the uretero-pelvic junction was probably the etiological factor in the production of the calculous pyonephrosis.

Case IX (G. U. 1,23A), J. M., male, 41 years of age, married, tin worker, was seen in consultation for the first time on Nov. 28, 1930. He had been admitted to the hospital 12 days previously complaining of sharp pain in the right upper quadrant. Onset of present illness dated back 13 years at which time he had developed sharp pain in the right upper quadrant which radiated across the abdomen and up the right shoulder. The pain was accompanied by chills, fever, and nausea, but no vomiting. He had frequently passed "gravel" about the size of a pea and had been told he had pus in his urine. He had hematuria at least once a year which preceded or followed the passage of a stone. He also complained of dysuria, burning, and frequency during the attacks. The attacks of pain recurred at intervals of two or three days. The pain recurred with increasing severity and frequency and was attended by marked gastro-intestinal symptoms. He consulted a surgeon, who made a diagnosis of cholelithiasis and advised hospitalization.

Physical examination was essentially negative except for an ill-defined, slightly tender mass in the right upper quadrant. The urine contained from 30 to 40 pus cells and from 20 to 30 red blood cells per h.p.f.

On Nov. 19, 1930, an exploratory laparotomy was performed. The gall bladder, stomach, and intestines appeared normal. In the right renal region there was a large mass, about the size of a child's head, which was interpreted as an enlarged kidney. Ten days later cystoscopy and pyelography revealed a non-functioning calculous pyonephrosis on the right side with four irregular calcified shadows within the kidney (Fig. 9).

On Dec. 12, 1930, a right nephrostomy was performed and about one quart of thick green pus was removed. No stones could be palpated within the pyonephrotic cavities although several of the cavities were lined with calcareous material which had a gritty sensation against the exploring finger. A thoracotomy was done on Feb. 20, 1931, after which the patient developed a draining sinus leading to the pleural cavity and another leading to the kidney. On Aug. 18, 1931, a right nephrectomy was performed, after which he made an uneventful recovery except for a persistent fistula at the operative site. On Sept. 14, 1933, a right ureterectomy and removal of necrotic tissue in the renal bed was performed in order to clear up the persistent renal fistula. The patient died twelve hours after the operation.

Histological study of the kidney revealed a heavy deposition of calcium salts in degenerative tissues containing evidences of acute and chronic fibrosis. There were no evidences of tuberculosis in any portion of the kidney.

Case X (G. U. 2,931), L. R., female, 33 years of age, married, housewife, was referred for examination on July 13, 1925, with a complaint of pain in both kidney regions. The patient had enjoyed good health until three years before, when she developed in the right side a sharp and colicy pain which radiated to the right lower quadrant. Pain recurred at frequent intervals. About a year before, she had hematuria during one of the attacks; she also had an occasional dull pain in the right kidney region. Examination disclosed tenderness in both kidney regions, more marked on the left than on the right. Catheterized specimen of urine showed many pus and red blood cells. Cystoscopy and pyelography revealed a calculus in the pelvis of the left kidney and several small shadows near the periphery of the kidney. Pyelograms showed the larger shadow to be within

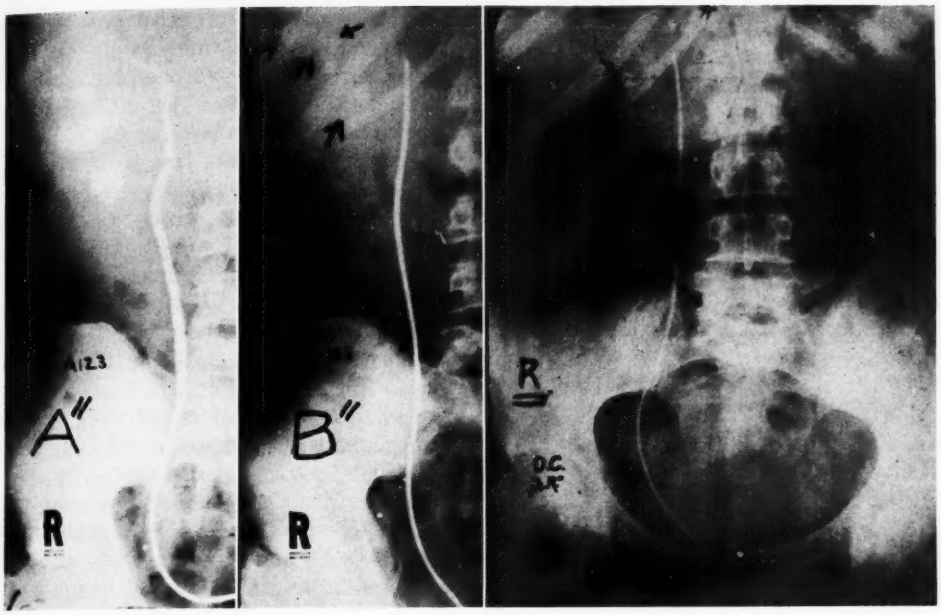

Fig. 9 (*left*). Case IX. In the plain roentgenogram ("B"), the arrows point to four irregular calcified shadows scattered through the upper part of the right kidney. In the pyelogram ("A"), the dye fills several large abscess cavities and obscures the calcified shadows. At operation the abscess cavities in the upper pole of the kidney were found to be lined with a calcareous material which imparted a gritty sensation to the exploring finger; no calculi were found.

Fig. 10 (*right*). Case X. A plain roentgenogram with catheter in right ureter. In the left kidney area, the arrow indicates a large calculus beneath which are seen several smaller calcified shadows in the parenchyma. At operation a large stone was found in the pelvis and several healed calcified abscesses. The shadow in the right kidney is a calculus which subsequently passed into the ureter and was removed by operation.

the pelvis and the small shadows to be within the parenchyma (Fig. 10). On Aug. 4, 1925, a left pyelolithotomy was performed, at which time several small calcified abscesses were noted in the lower pole of the kidney.

On July 30, 1926, the patient was found to have a large calculus in the right ureter with an infected hydronephrosis on the right. She received several treatments and passed the stone in the right ureter. On March 8, 1929, cystoscopy and pyelography revealed a non-functioning pyonephrotic right kidney, with several irregular calcified shadows in the parenchyma of the kidney. On March 12, 1929, the left kidney was removed and showed extensive destruction of the pelvis, calices, and parenchyma. Many large abscesses were scattered throughout the kidney, several of them containing fine calcareous particles. Histological study showed extensive, acute and chronic pyelonephritis and pyonephrosis.

Case XI (G. U. 2,927), J. L. C., 39 years of age, male, married, confectioner, was referred for examination on July 7, 1925, with a complaint of symptomless hematuria. Voided specimen of urine showed an occasional pus cell and red blood cell.

Cystoscopy and pyelography were performed on July 9, 1925. Plain roentgenogram revealed an irregular calcified shadow in the lower pole of the left kidney. The stereoscopic pyelograms showed the shadow in question to be situated in a pyramid immediately adjacent to the lower major calyx. A tentative diagnosis of renal calculus or calcification of the tuberculous abscess was made. Bacteriological study

and guinea pig inoculation were negative for tubercle bacilli. A left pyelolithotomy was performed on April 1, 1932, and two years later the same kidney was removed.

The left kidney showed numerous abscesses throughout its cortex. On cross-section, a large stone was found in the pelvis, extending into the upper major calyx. There were numerous abscesses throughout the parenchyma, several of which contained calcareous material in the inspissated pus lining the walls of the abscessed cavities. Histological study showed acute and chronic pyelonephritis, with calcification in the walls of abscess cavities.

(C) Tumors of the Kidney—1. Cystic Lesions

(a) Solitary Cysts.—The occurrence of calcification in the walls of a serous hemorrhagic cyst is a relatively uncommon finding. In 1885, Morris reviewed 2,610 autopsies at the Middlesex Hospital and found five solitary cysts, one of which, the size of a horse chestnut, observed in a 19-year-old patient, had calcified walls. In 1902, Albarran and Imbert stated that the fibrous walls of renal cysts may be infiltrated with calcium salts, but they presented no case reports. Haenisch is quoted by Arkin and Lepehne as reporting the first case of calcified cyst, in a 65-year-old male. The first report of a calcified cyst in the English literature was made by Case in 1915. The following year, Cunningham reported two calcified cysts in a series of 29 cases of small solitary cysts in the autopsy records of two Boston hospitals. Clute (1916) observed necrosis and secondary calcification of the cyst wall in two cases operated upon. In addition to the above cases, we have collected 22 cases from the literature, as follows: Israel and Israel (1925); Laquiere (1925); Kirwin (1926); Day (1928); Joseph (1928); Kairis (1928); Latteri (1930); Byrum (1931); Colston (1932), 6 cases; Damm (1932); Melly (1933); Jones (1934), 2 cases; Herbst and Vynalik (1935); Barney (1936); Herskovitz (1936), and Mohr (1937). Several of the cases reported by Colston are also published in Young and Waters' monograph on Urological Roentgenology; one of these cases was a personal case of the authors and is herewith reported in brief.

The etiologic rôle of trauma in the production of these calcified cysts is clearly demonstrated in the cases reported by Herbst and Vynalik, Day, and Colston. Colston was of the opinion that these calcified cysts arise in one of two ways: either (*a*) from hemorrhage into a simple serous cyst, or (*b*) from the natural evolution of a perirenal hematoma. He maintained that calcification occurs as a result of degenerative processes which take place when the extravasated blood is not absorbed, *viz.:* the blood within the cyst coagulates, clots, and adheres to the walls of the cyst, and calcium salts are precipitated from the organized blood clots.

Case XII (G. U. 3,089), S. B., white, male, 55 years of age, married, tailor, was admitted to the Sinai Hospital on the service of Dr. Goldstein on Feb. 2, 1926, complaining of a large mass in the right side of the abdomen and inability to walk properly. Twenty-five years previously the patient had been kicked by a horse in the right flank. Following this, a mass had appeared in the right flank which became slowly progressive in size but caused no distress until about six months before the patient came to us, when it began to interfere with locomotion. The patient had had no urinary symptoms.[1]

On physical examination a solid irregular mass could be felt, extending across the mid-line, 5 cm. below the crest of the ilium and upward underneath the costal margin. This mass was fixed, firm, and did not descend on inspiration. The urine was clear, negative chemically and microscopically. A plain x-ray film showed three huge, apparently intercommunicating cysts, with irregular areas of calcification in the walls, with a deep septum between the larger cysts. No kidney structure was visible (Fig. 11). At operation,

[1] For full details of this case, see Colston's article.

the kidney, with the tremendous cyst closely adherent to its posterior border, was removed. Death occurred twenty-four hours after operation.

(*b*) *Echinococcus Cyst.*—Retrogressive changes predisposing to the deposition of calcium salts may occur in other cystic diseases of the kidney. In the earlier textbooks of Rayer, Roberts, and Dickinson, mention is made of the occurrence of calcification in the walls of acephalocysts, *i.e.*, hydatid cysts. In the recent literature there are numerous reports of hydatid cysts, many of which showed calcification. Those interested in this phase are referred to the excellent contributions of Craig and Lee-Brown, Racic, Blum, Koch, Young and Waters, and others.

(*c*) *Perirenal or Peripelvic Cysts.*—Among the rare cystic diseases of kidney and surrounding tissues in which calcification has also been observed are peripelvic cysts, perirenal cysts, and multilocular cysts of the kidney. Israel and Israel (1925) reported an unusual case of nephrolithiasis accompanied by two calcified peripelvic cysts, the size of a plum and cherry, respectively. Colston has described calcification in the walls of perirenal cysts following injuries to the kidney. Wesson (1930) reported a case of multilocular cyst of the lower pole of the left kidney with calcareous degeneration of the walls of the cysts. Winsbury-White (1932) reported a case of stone in the ureter, accompanied by shadow-casting nodules of degeneration in the corresponding atrophied kidney, in a female 29 years of age. He considered the calcified nodule to be the result of degenerative changes in a cyst, a finding which was further substantiated by the presence of a thick hyaline capsule.

(*d*) *Polycystic Diseases.*—A careful search of the literature has revealed an occasional report of calcification of a congenital polycystic kidney. Gruber (1925) stated that calcification may occur in the walls of the cysts in this condition, and cited the observations of Douilland (1827) and Lohman (1853) on the deposition of calcium salts and uric acid in the tubules situated between the cysts. Domrich (1934) reported a case of calcified cysts diagnosed by roentgenographic examination. Small deposits of calcium were found in the walls of several smaller cysts located near the renal pelvis. The calcification was attributed to degenerative changes of organized blood clots within the cysts.

Fig. 11. Case XII. Plain roentgenogram showing a large multilocular calcified cyst of the right kidney.

Case XIII (G. U. 1,868), C. P. L., male, 45 years of age, married, merchant, was admitted to Sinai Hospital on Feb. 3, 1936, with the complaint of pain in the left upper quadrant and progressive weakness. He did not complain of any urinary symptoms. On examination of the abdomen, a large irregular mass was found in the left quadrant and a smaller mass in the right upper quadrant. The urine, which had a specific gravity of 1.008, gave a positive test for albumin and showed an occasional pus cell.

Cystoscopy and pyelographic study revealed the typical changes of bilateral

polycystic disease but no areas of calcification were seen. A nephrocutaneous fistula was established. At the time of operation, several small calcareous bodies, varying in diameter from 1 to 3 mm., were found within some cysts, and in several areas calcium deposits were found lining the walls of cysts and in the interstitial tissue between cysts. Several pieces of tissues were removed for study and showed the typical histological changes of polycystic disease.

(*e*) *Congenital Cyst.*—Uthoff (1936) reported a unique case in a female, four years of age, who had a solitary right kidney with a calcified renal cystic vestigial remnant which was seen in the roentgenogram and interpreted as a large pelvic calculus. At operation, a calcified cystic mass was delivered and extirpated. The mass was attached to the kidney by fibrous tissue and was completely devoid of any blood supply. No evidence of renal epithelium could be demonstrated.

(*f*) *Dermoid Cyst.*—Calcification may also occur in dermoid cysts of the kidney. Valentine (1929) reported one case and collected eight cases from the literature: in four, cholestrin crystals were found; in six, an indefinite substance of varying color and consistency, often containing deposits of calcium salts, was found within the cysts or in the cyst walls. Fahre (1934) reported a dermoid cyst of the kidney which showed calcification on the roentgenogram.

2. Benign Tumors.—In the older literature occasional mention is made of hyalinization and calcification in tumors of the renal capsule, *i.e.*, adenoma, fibroma, myoma. In 1908, Nurnberg reviewed a large series of benign renal tumors which included lipoma (7 cases), fibroma of capsule—*markfibroma*—(67 cases), fibromyoma and lipomyoma (122 cases), myosarcoma (13 cases), adenoma (66 cases), and angioma (4 cases). He observed calcium deposits within the tumor mass in the capsular fibromatous and adenomatous type of tumor. He also observed the frequent occurrence of calcium deposits in the non-tumor-bearing areas of the kidney. One patient had two distinct tumors, namely, a fibroma of the capsule and a calcified cyst adenoma. Arkin (1926) stated that he had seen such cases at postmortem, but gave no further details. Fahr described calcium deposits in a tubular adenoma, the size of a walnut, in a patient with pulmonary tuberculosis.

3. Malignant Tumors.—The attention of the urologists and roentgenologists was drawn to this interesting pathological change by Arkin's report, in 1926, of a case of calcification of a hypernephroma diagnosed by roentgenographic study. Prior to this report, experience with this pathological phenomenon was limited to the report of an occasional case observed at autopsy. The treatises on renal tumors by Albarran and Imbert and by Garceau fail to mention the presence of calcification in renal tumors.

(*a*) *Hypernephroma.*—Calcification of the tumor tissue is most commonly observed in the so-called hypernephroma. The earliest report is by Albrecht (his Case 25), in 1905, who described pathological features of a hypernephromatous left kidney removed from a 58-year-old woman by Hochenegg, in 1903. He found two tumor masses in the lower pole of the left kidney: the lower mass, about the size of an apple, was surrounded by a dense calcified capsule; the second smaller tumor, nearer the pelvis, was surrounded by a dense fibrous capsule which was calcified in some places.

In 1908, Hall reported a case of hypernephroma (his Case XIII) in which an unusual degree of calcareous degeneration existed, but the pathological description was very meager. Pleschner (1914) presented a clinical and pathological study of 25 cases of hypernephroma and found only one case (his Case X) with calcification. This patient, 32 years old, had a large tumor in the left kidney region which was considered to be a large area of hydronephrosis, but, at operation, a hypernephroma was found and removed. Pathological study revealed deposits of calcium,

varying in size from a millet seed to a pea, in several portions of the tumor near the surface. Lorraine (1915) reported a case of calcification of a hypernephroma in the upper pole of the right kidney in a 20-year-old male. The calcification was present in the form of three indurated calcified planes in the lower portion of the tumor near the adjacent tissue.

Arkin reported the first case of calcification in a hypernephroma in which an accurate diagnosis was made by roentgenographic and fluoroscopic study and confirmed by operation. In 1921, one of us (A. E. G.) diagnosed a case of calcification and ossification in a hypernephroma by roentgenographic studies. This case was not reported at that time but is included in the present series of cases.

Following this report, cases of calcification in hypernephroma were reported with greater frequency as evidenced by the reports of Braasch, Kretschmer, Keen, Lepehne, Ray, Ravich and Turkeltaub. Braasch and Griffin found roentgenographic evidence of calcification in seven cases. In a personal communication to Keen, Braasch stated that he has observed at least 15 or 20 cases of hypernephroma with roentgenographic evidence of calcification. Arkin and Braasch have emphasized the importance of differentiating these shadows from those caused by renal calculi and tuberculosis. Renal calculi and tuberculosis can usually be excluded by the absence of any clinical, cystoscopic, or urographic data characteristic of these conditions. Braasch suggested that the roentgenographic diagnosis of neoplasms can be inferred by the presence of coincident areas of calcification and unipolar irregularity of the renal outline.

Hypernephromas containing both calcified and osseous tissues have been reported by Pocharissky, Gierke and Frankel, Brugnatelli, Baroni, Arkin and Moro. Calcification of a pseudo-cyst with a hypernephroma has been described by Lepehne. A similar case with osseous changes was reported by Fabricius. Kraft observed a degenerated cystic and calcified hypernephroma in a woman aged 46 years.

Keen reported an unusual case of right renal tuberculosis and left calcified hypernephroma in a 63-year-old man. A diagnosis of left renal tuberculosis was made by an urologist because of the presence of large calcareous deposits in the left renal region. A roentgenogram taken five years later showed no evidence of the calcareous deposits noted previously. At autopsy two years later, the left kidney, previously diagnosed as tuberculous, was the seat of an extensive hypernephroma containing calcium deposits. Smears taken from the tumor mass were negative for tubercle bacilli. The right kidney was tuberculous and contained a metastatic hypernephromatous nodule in the pelvis.

The pathogenesis of calcification in hypernephroma may be readily explained on the basis that this tumor may be present for many years before giving rise to symptoms, and during this long course degenerative and retrogressive changes may occur within the tumor which eventually result in calcification or even osseous metaplasia. These degenerative changes, namely, necrosis, hemorrhage, cystic degeneration, are usually present to some degree in every hypernephroma, but the extent of these changes appears to vary with the size and rate of growth of the tumor.

In the alveolar or papillary type of hypernephroma containing a scant amount of connective tissue, a large pseudo-cyst may develop as a result of necrosis and cystic degeneration. In the solid type which is composed of densely packed nests of cells separated by connective tissue septa or surrounded by capillaries or blood sinusoids, one may detect areas of fresh hemorrhage in the midst of hypernephroma cells; also large and small cysts lined with organized blood clots or blood pigment. As a result of these pressure and vascular changes, the microbiotic process involves the tumor mass and its capsule and secondary metaplastic changes, namely, hyalinization, calcification, and,

Fig. 12 (*upper left*). Case XIV. Pyelogram of left kidney showing compression, elongation, and distortion of the lower major calyx produced by a hypernephroma. The arrow points to a calcified shadow in the lower portion of the tumor mass. The favorable prognostic significance of calcification in hypernephromas of the kidney is substantiated by the fact that this patient enjoyed good health for seven years following nephrectomy, but in the eighth year developed parotid, orbital, and pulmonary metastases which proved fatal.

Fig. 13 (*upper right*). Case XV. Pyelogram showing obliteration of the upper major calyx and compression and distortion of the middle major calyx due to a hypernephroma of the upper pole of the right kidney. The arrow indicates an area of calcification in the tumor mass.

Fig. 14 (*lower left*). Case XVI. Pyelogram showing the characteristic deformities of the pelvis and calices produced by a hypernephroma in the upper pole of the right kidney. The arrows indicate two large calcified shadows present in the periphery of the tumor.

occasionally, ossification, ensue. The calcium deposits are usually irregular in consistency and confined to one or two areas. In rare instances of long-standing tumors, the calcification may be scattered throughout the entire tumor.

Braasch is of the opinion that calcification is a favorable sign inasmuch as, of the seven patients with calcification in hypernephroma observed by him, all but one lived more than three years and four were alive at the end of five years. One of the authors' patients lived 11 years after operation. Ray interpreted the calcification in a case of hypernephroma as evidence of spontaneous regression. Rohdenburg recently collected 302 cases of so-called spontaneous recession of malignant tumors, several of which were hypernephroma, and stated that necrosis with calcification is the most common type of degeneration associated with recession of malignant tumors.

Case XIV (G. U. 75), M. R., male, 56 years of age, married, tailor, was admitted to the Sinai Hospital on Nov. 14, 1921, with a complaint of pain in the left upper quadrant. There were no urinary symptoms other than a slight frequency. On examination, a round firm mass was found in the left upper quadrant; it was not tender and moved with respiration. The urine was negative. The plain roentgenogram and pyelogram showed an irregular crescentic calcified shadow in the lower pole of the kidney which did not resemble a calculus. In the pyelogram, the calcified shadow appeared to be in the periphery of a tumor situated in the lower pole of the left kidney (Fig. 12). A pre-operative diagnosis of calcification of hypernephroma was made.

On Nov. 18, 1921, a left nephrectomy was performed; convalescence was uneventful and the patient was discharged on Dec. 8, 1921. The operative specimen showed a large tumor, of firm consistency and yellowish-orange in color, which had occupied the lower pole of the kidney. On cross-section several areas of hemorrhage and cystic degeneration were observed. A stony hard, whitish plaque which could not be cut with a knife and required the use of a saw, was encountered at the periphery of the tumor. Microscopic studies revealed typical hypernephromatous changes. The stony hard area was decalcified and showed the characteristic histological evidences of calcification and ossification.

The post-operative course of this patient was extremely interesting and we were fortunate that he remained under our observation until his death. He continued to enjoy good health until May 9, 1928 (approximately seven years after operation), when he was found to have a nodular mass (3 × 2 cm.) at the tenth costochondral junction on the right side and a slightly smaller nodule about the size of a pecan in the left parotid region. The former nodule was removed and showed characteristic histological structure of a hypernephroma. On June 11, 1928, he developed metastasis in his right orbit, causing a marked exophthalmos with loss of vision in that eye. A roentgenogram of the chest, taken on July 11, 1928, revealed metastases to his lungs for the first time. He died on Feb. 9, 1929, of progressive cachexia.

Case XV (G. U. 3,927), A. M., male, 52 years of age, married, clerk, was first seen by us on Oct. 12, 1928, complaining of pain in the right renal region of one month's duration. His family and past histories were negative. About one month before, he developed an attack of dull pain in the right lumbar region, radiating to the right groin, which lasted about nine hours and was unaccompanied by urinary symptoms. Two weeks before, he had a similar attack of pain which lasted only

Fig. 15 (*lower right*). Case XVII. Unilateral pyelogram showing the filling defect (*B*) produced by a tumor in the lower pole of left kidney. No dye was injected into the right kidney. The calcified shadows in the region of the right kidney, indicated by arrows (*A*), were originally considered to be gallstones. This film was taken on Jan. 18 1927.

two hours but which was accompanied by urgency, frequency, and hematuria.

Physical examination was negative except for a round smooth mass in the right upper quadrant about the size of a large grapefruit. A voided specimen of urine was negative for albumin and sugar and microscopically showed three to four pus cells per h.p.f. A tentative diagnosis of hypernephroma was made which was confirmed by cystoscopy and pyelography. The plain roentgenogram showed a calcified shadow in the region of the upper pole of the right kidney, while the pyelogram showed compression and distortion changes in the upper and middle major calices, typical of a renal tumor. The calcified shadow was situated within the tumor mass (Fig. 13). On Oct. 19, 1928, the right kidney and tumor were exposed through a lumbar incision and the condition was found to be inoperable. The ureter was ligated. The patient made an uneventful recovery. Following discharge from the hospital, he became progressively weaker and died on April 26, 1930.

Case XVI (G. U. 6,672), M. B., female, 50 years of age, married, housewife, was admitted to the surgical service of the Sinai Hospital on May 30, 1933, with the complaint of dull pain in the right upper quadrant of six weeks' duration. The urine was negative except for an occasional pus cell. A tentative diagnosis of chronic cholecystitis was made.

On June 5, 1933, an exploratory laparotomy was performed but the gall bladder and gastro-intestinal tract appeared normal. A large mass about the size of an adult's head, considered to be a hypernephroma, was palpated in the right kidney region. She was discharged from the hospital on June 21, 1933, and referred to the urological out-patient clinic for further study.

Several weeks later, cystoscopy and pyelography confirmed the diagnosis of a renal tumor. The plain roentgenogram and pyelogram showed an irregular dense calcified shadow in the upper pole of the kidney in the region corresponding to the periphery of the tumor (Fig. 14). The tumor was considered to be inoperable despite the absence of demonstrable metastatic foci in the lungs and long bones, and a course of intensive roentgen irradiation was instituted on July 3, 1933, and carried out at regular intervals over the next three years. In July, 1933, roentgenogram of the lungs and long bones again failed to reveal any metastases. Despite deep roentgen therapy, metastatic foci were demonstrable in the lungs and ribs in August, 1935, and in the cervical vertebræ in August, 1936. The patient became progressively weaker and succumbed in October, 1936.

Case XVII (G. U. 526), E. W., male, 63 years of age, married, salesman, was admitted to the Sinai Hospital on Jan. 10, 1938, complaining of increasing weakness, dyspnea, precordial pain, and pain in the right flank for the past eight months. The pain in the right flank was of a severe, gnawing character and persistent. He had lost 18 pounds in weight during this time. There were no urinary difficulties other than slight frequency. His past history was interesting inasmuch as on Jan. 25, 1927, his left kidney, which contained two encapsulated tumor masses in the lower pole, had been removed. Each tumor was approximately 5 cm. in diameter and histologically showed the characteristic structure of a hypernephroma. The pre-operative diagnosis of left renal neoplasm was based on the history and physical findings, and was confirmed by pyelography. Unfortunately no pyelographic studies of the right kidney were made, although the calcified shadows in the right kidney area were noted but were considered to be gallstones (Fig. 15). Following the operation, the patient enjoyed good health until the present illness.

Physical examination was essentially negative except for the abdomen, which contained a large round mass, about the size of a grapefruit, in the right upper quadrant. The mass was firm, tender, but

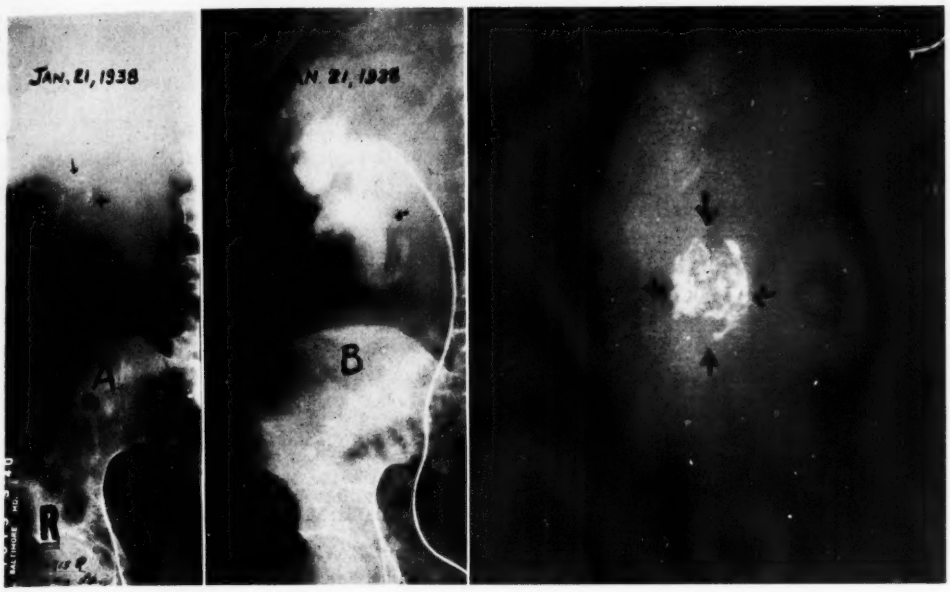

Fig. 16 (*left*). Case XVII. The area of calcification in the right kidney, observed in 1927, is present in the plain film (*A*), taken exactly 11 years later. There is no apparent increase in the size of the shadow. The right stereoscopic pyelogram (*B*) shows a marked dilatation of the pelvis and calices, with distortion of the pelvis and lower calices by a tumor mass on the posterior surface of the kidney. The calcified area appeared to be in the central portion of the tumor mass.

Fig. 17 (*right*). Case XVII. A roentgenogram of the right kidney and tumor, obtained at autopsy, shows the area of calcification to be in the center of the tumor mass

not fluctuating. The urine showed a faint trace of albumin and contained an occasional pus cell. Intravenous pyelography failed to show any dye in the right kidney area after 40 minutes. However, in the right kidney area there was noted a large round shadow, extending from the twelfth rib to the iliac crest, within which was a calcified area comparable to that observed 11 years previously (Fig. 16-*A*). The outline of the right kidney appeared to be superimposed upon the larger shadow. A stereoscopic retrograde pyelogram revealed a marked dilatation of the pelvis and calices, with elongation and distortion of the lower calices and pelvis. The kidney appeared to be anterior to the tumor mass and the calcification was adjudged to be within the tumor (Fig. 16-*B*). A diagnosis of renal neoplasm with calcification was made.

During his stay in the hospital, the patient developed a progressive uremia. The phthalein declined from 10 to 3 per cent for two hours and the blood urea rose from 76 to 170 mgm. per cent. The patient died on Jan. 26, 1938. Autopsy disclosed a large hypernephroma (12 × 10 × 8 cm.) on the posterior surface of the kidney with metastases to the liver and spleen. The area of calcification was found in the central portion of the tumor (Fig. 17).

In retrospect, it appears that the right renal neoplasm was present at the time the left kidney was removed but unfortunately was not diagnosed. The calcification in the center of the right renal neoplasm apparently did not increase materially in size during the 11 years following the operation. Since the patient had not had any roentgenographic studies prior to the operation in 1927, it is impossible to state exactly how long the calcification had been present, but certainly one may state that its presence in this case was a

favorable sign. The question as to whether we were dealing with bilateral primary renal neoplasm or with a primary neoplasm in the right kidney, with secondary or metastatic involvement of the left kidney, must remain a matter of conjecture until further histological studies of both tumors are made.

(*b*) *Other Malignant Tumors* (*Carcinoma, Sarcoma, Mixed Tumors, Myoma, etc.*).—Calcification has also been observed in other types of renal tumors. Keen (1889) reported a case of an "encephaloid" carcinoma of the kidney, with calcified blood vessels, which simulated renal calculi. Kischensky observed a calcified squamous-cell carcinoma of the kidney with multiple metastases. Loumeau (1910) observed a case of calcified renal carcinoma which simulated tuberculosis. Grosglik (1911) described a case of calcified blood clot in the center of a carcinoma of the left kidney, which was mistaken for a renal calculus. In 1930, Federoff observed calcification in a tumor (sarcoma?) of a supernumerary kidney. Crosbie and Pinkerton (1932) reported a case of malignant myoma of the kidney which showed histological evidences of early calcification. Recently Rosenberg reported two cases of adenoma of the adrenal gland associated with a hypernephroma. In each instance the hypernephroma showed areas of calcification.

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A ROENTGENOLOGICAL STUDY OF PINEAL ORIENTATION

II. A COMPARISON OF THE GRAPHIC AND PROPORTIONAL METHODS IN PROVEN CASES OF BRAIN TUMOR

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IN a previous communication, (1) the comparative accuracy of the original graphic method of pineal localization of Vastine and Kinney (2) and the proportional method recently devised by the writer was determined in 104 cases of normal skulls. The graphic method was derived in 1927 by directly plotting the position of the gland in respect to selected points on the calvarium with a corresponding diameter of the skull on graph paper and delimiting a normal zone after a study of known normal cases. The method when analyzed is found not to be a proportional method, *i.e.*, the distance of the pineal from the calvarium does not vary directly with the size of the skull. The proportional method[1] which we have devised is based on strict proportionality and does not require any direct measurements of the film nor does it require a graph for its interpretation, a mechanical guide

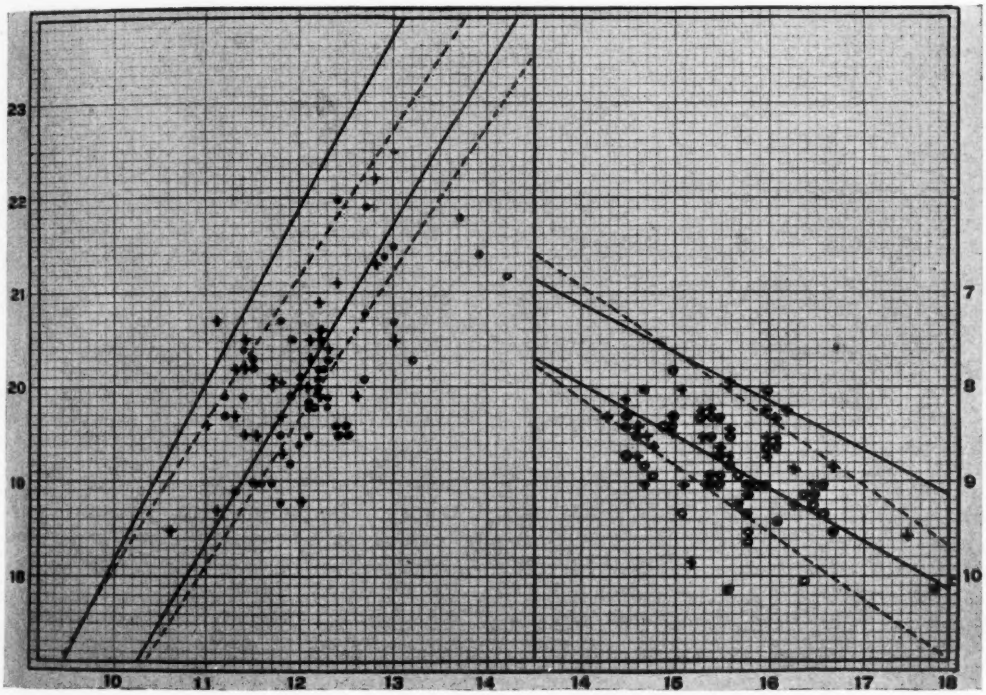

Fig. 1. Distribution of pineals in a series of 64 brain tumors arising within the cerebral lobes, comparing the graphic method (broken lines) with the proportional method (solid lines). Symbols: ○ = frontal; + = temporal; ● = parietal. The proportional method shows a greater number of cases with displaced pineals (posterior or downward displacement).

[1] Since paper's completion, the writer has learned that J. D. Camp, M. D., of Rochester, Minn., exhibited before the College of Radiology in 1933, a pineal localizer employing a coil spring with proper markers. In a personal communication he states that he did not publish a description of his device because of manufacturing costs. It is of no little interest to note, however, that the underlying principle of his device is similar to the writer's proportional method—the uniform stretching linearly of a calibrated material.

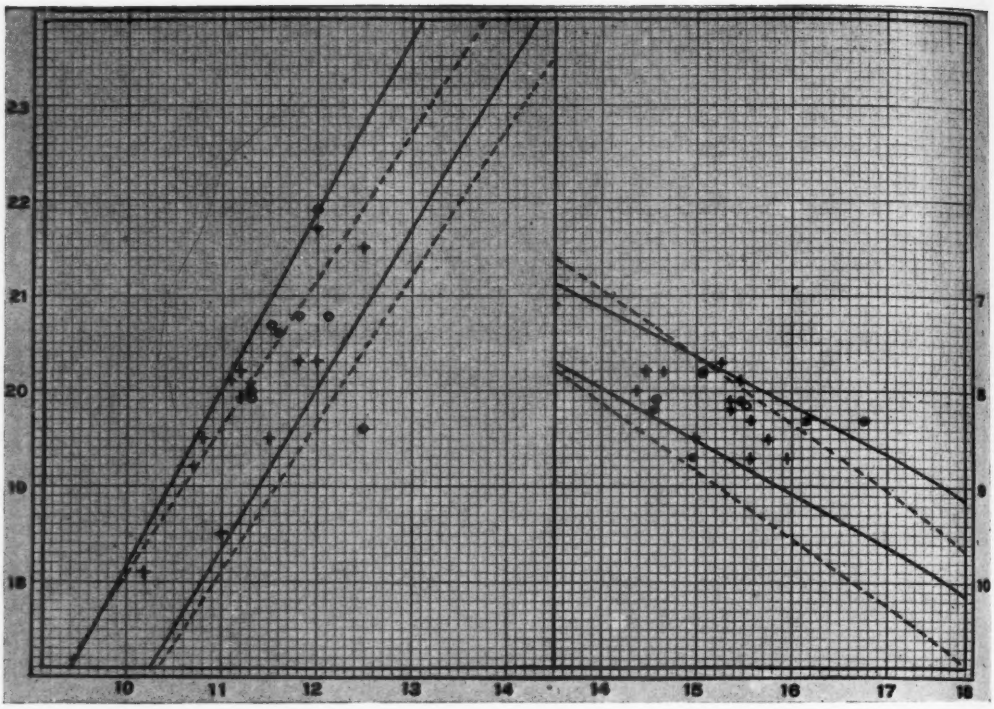

Fig. 2. Distribution of pineals in 21 cases of tumors of posterior fossa, comparing graphic method (broken lines) with the proportional method (solid lines). Symbols: ○ = cerebellar lobes; + = petrous pyramid; ● = fourth ventricle.

serving for a direct reading of the pineal position by holding the guide against the skull film. The differences in the two methods have been described in some detail in the communication mentioned above. In the normal series, the position of the pineal was found to be interpreted correctly in approximately 84 per cent of these cases by the graphic method and in 92 per cent by the proportional method for measurements relating to the antero-posterior diameter and 89 per cent and 93 per cent for measurements relating to the vertical diameter.

To complete this study, the records of all verified cases[2] of brain tumor were reviewed and 147 cases were found suitable for analysis, *i.e.*, cases in which the pineal was calcified sufficiently to enable one to identify its position with certainty, and the brain tumor was verified either by operation or autopsy. All tumor unverified cases or tumor suspects were eliminated from the series.

For analysis the series was first divided according to the location of the tumor within the brain. Tumors of the frontal or parasagittal region (anterior portion) most frequently of all cerebral lobe tumors produced a pineal shift which could be detected by measurement of the lateral film (Fig. 1). Of 37 cases of frontal tumors, the pineal in 17 cases was found in normal position when the graphic method was employed and in only nine when the proportional method was used. The most common direction of displacement was posterior. Displacement downward without a simultaneous backward shift was distinctly uncommon, while a combination of two displacements was very common,

[2] The writer is indebted to Dr. W. P. Van Wagenen, of the Neuro-surgical Division, who generously extended the use of his records, from which was selected a list of all verified cases of brain tumor up to the year 1936. The use of those records greatly facilitated the classification and verification of this series of brain tumors.

particularly when the proportional method was employed. Displacement, inferior or posterior, was identified in 18 out of 37 cases (approximately one-half of the cases) by the graphic method, and in 28 out of 37 cases (approximately three-fourths of the cases) by the proportional method. The graphic method gave a paradoxical result in one case in which anterior displacement was indicated. A lateral shift from the midplane of the skull was identified in slightly over half the cases of frontal tumor (56 per cent). The question might arise whether a frontal tumor can be present as a space-occupying mass within the frontal region which cannot be detected by measurements of either the anteroposterior or lateral skull films. This can occur and was noted in three cases of this series. It is uncommon, however, and a finding of a normally placed pineal on both the anteroposterior and lateral skull films makes a tumor of this region unlikely if the proportional method is used in measuring the lateral films and the measurements of the anteroposterior film are made in the manner described in a previous communication (3).

Tumors arising within the other lobes of the cerebrum (chiefly temporal or parietal tumors) less commonly produce displacements which can be detected from an analysis of the lateral film. When displacement was present, the direction of the displacement was either backward, downward, or a combination of the two as in frontal tumors. Forward displacement was not observed even in cases of tumor located as far posteriorly as the parietal region. The few occipital tumors which have been verified in our clinic have not shown calcified pineals except in one instance, and we have very little information relative to the type and frequency of pineal shifts in these uncommon tumors. In our series, tumors in the temporal or parietal lobe are much more apt to produce a lateral shift from the midplane position than in cases of frontal tumor. In 18 cases in which the pineal could be identified on the anteroposterior film, lateral displacement was found in all.

Cerebellar tumors commonly show no consistent type of displacement which can be detected by measurement of the lateral skull film (Fig. 2). In the few cases in which displacement was indicated, the direction of the displacement was upward or upward and forward. Six out of 21 cases were found displaced in this manner by the graphic method and three by the proportional method. In the two cases in which forward displacement alone was noted, it became doubtful if this displacement was real, since the skulls of these two cases were dolicho cephalic, a condition recognized as a frequent source of error when the graphic method is employed. Such forward displacement was absent if the proportional method was used. There was a single case in which the displacement appeared paradoxical, the pineal being shifted posteriorly by both the graphic and proportional methods. A more detailed examination of this case indicates a possible explanation of this finding. The sella was enormously enlarged, with marked erosion, and associated with it was a pronounced dilatation of the third ventricle. It is quite possible that the enlarging ventricle had pushed the pineal backward at its posterior margin in the direction of the tumor. A lateral shift of the pineal from the midplane is not observed in cerebellar tumors.

Sellar tumors and tumors about the third ventricle may show the pineal outside the normal zone occasionally (Fig. 3). The former tend to place the gland above the normal zone and at times in front of it, while those about the third ventricle may displace the gland backward and downward. The enlarging and changing shape of the head in pituitary disease may account to a major degree for the apparent displacement of the pineal. The pituitary in enlarging could not produce an actual shift of the pineal forward in the direction of the tumor, but the changing shape of the head might result in an apparent shift. A lateral shift from the mid-

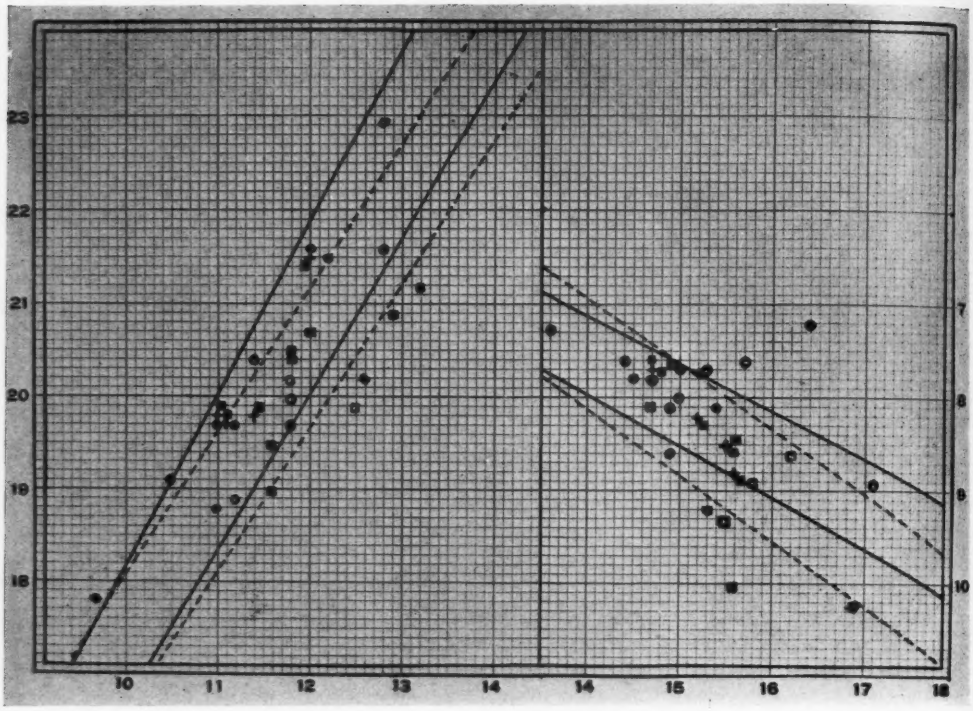

Fig. 3. Distribution of pineals in 31 cases of midline tumors of the brain, comparing graphic method (broken lines) with the proportional method (solid lines). Symbols: ○ = pituitary; ● = suprasellar; + = aneurysm of circle of Willis; □ = pineal; ■ = third ventricle.

plane of the skull is usually absent, because of the midline location of the main mass of the tumor.

Tumors arising within the pineal would not at first glance appear to be capable of displacing the parent organ. However, because of its strategic position at the mouth of the aqueduct of Sylvius and its proneness to produce a dilatation of the third ventricle, secondary to blockage at this level, a crowding backward of the pineal may result. This occurred in two of our cases.

Fluid at the surface convexities of the brain does not commonly produce any recognizable shift of the pineal on the lateral film, but the anteroposterior film becomes important because not infrequently the pineal may be found to the right or left of the midsagittal plane. Tumors of the choroidal plexus and aneurysms of the arteries at the circle of Willis do not reach a physical size, as a rule, to permit identifying a pineal shift. On the other hand, a midline mass or tumor such as a cyst of the septum pellucidum may displace the pineal both downward and backward. In the few cases of our series of these miscellaneous types, the findings by the graphic and proportional methods were practically identical.

Dividing our tumors according to cell types of origin, of the gliomas (59 cases) 44 per cent were found displaced by the graphic method and 58 per cent by the proportional method by an analysis of the lateral films. On the anteroposterior films of these cases the pineal could be identified in approximately one-half of the cases. A lateral shift of the pineal was a very common finding, being noted in 20 out of the 30 cases. An analysis of the 10 cases showing no shift, the location of the tumor was as follows: two pineal, two

mesencephalon, one cerebellar, one corpus callosum, and four frontal. The reason for lack of displacement lies in the fact that

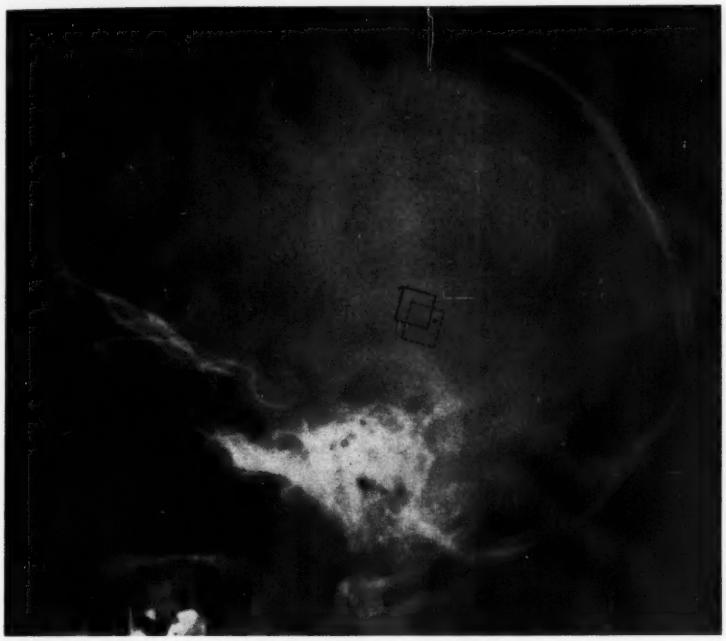

Fig. 4. Right frontal glioma. There were no reliable localizing signs clinically. An attempt at ventriculography was not successful. The pineal falls within the normal zone when the graphic method is employed (broken line). The proportional method indicates posterior displacement. The measurements of the anteroposterior films indicate a definite lateral shift (to the left).

many of these gliomas lie either at or close to the midline, often at the base of the cranium. The exception is found in frontal tumors, four of those showing no displacement (four out of 11 cases).

There were 26 cases of meningiomas in this series with calcified pineals; in 50 per cent of the cases the pineal was found displaced by the graphic method, and 58 per cent by the proportional method on the lateral film. A lateral shift to the right or left of the midline was a frequent finding, occurring in 10 out of 12 cases. Of the two cases showing no shift, one was located beneath the tentorium and the other arose from the tuberculum sellæ. Of the 10 cases noted displaced on the anteroposterior film, five, or one-half, showed a normal position on the lateral film. This emphasizes the importance of identifying the pineal on all anteroposterior or postero-anterior films whenever possible, repeating the films if necessary to secure this information. This film often gives the sole localizing information to be obtained during the routine examination of the skull.

In this series there were 11 neurinomas which characteristically showed no displacement of the pineal. However, in this form of tumor, the direct evidence of destruction of the apex of the petrous pyramid usually gives all the localizing information necessary. While displacement of the pineal was not evident from measurement of the anteroposterior and lateral skull films, exceptionally a displacement upward was evident (two out of 11 cases). The conclusions were essentially the same, whether the graphic or proportional methods were used, except that in two of the

longer skulls, the pineal lay in front of the normal zone by the graphic method.

Adenomas are restricted to the pituitary region. These tumors located at the sella have already been discussed. While there is an unexpectedly large number of pineals lying outside the normal zone, changes in head shape occurring in acromegaly account for many of these findings. Craniopharyngiomas usually occur at an age period during which the pineal remains uncalcified, and we have very little information concerning pineal displacement.

Metastatic tumors and tumors growing into the brain structures by direct extension may produce pineal shifts detectable on either the anteroposterior or lateral films. Metastatic tumors are commonly smaller in size than primary brain tumors, death supervening before massive growth results. In some cases of metastatic tumors including abscesses, the measurements of the pineal in the lateral film were normal but the anteroposterior film showed a shift of the pineal from the midsagittal plane.

Fig. 5. Right temporal glioma with clinical evidence of a left hemiparesis. The pineal does not appear displaced by the graphic method of Vastine and Kinney (broken lines), but appears displaced posteriorly by the proportional method.

Tumors of malignant origin arising within the orbit and growing by direct extension did not displace the pineal, but a carcinoma arising within the sphenoid did displace the pineal backward. A granuloma of the right frontal region behaved in much the same manner as a glioma, displacing the pineal backward and to the left of the midline. An osteoma arising within the frontal sinus produced sufficient bulk within the cranium to displace the pineal backward. The graphic and proportional methods gave similar results in this group of tumors, but in two of the longer skulls false results were obtained by the graphic method, forward displacement of the pineal being indicated with growths occurring within the frontal region.

Surface fluid at the convexities of the

brain, subdural hematoma, epidural abscesses, pachymeningitis hemorrhagia interna, often showed a lateral shift of the pineal in our cases and in several of them there was also evidence of a shift downward or backward. Accurate measurements of the anteroposterior film are of chief importance when unilateral fluid collections are considered, since these conditions commonly show only a lateral shift.

Fig. 6. Astrocytoma involving portions of right frontal, temporal, and parietal lobes. In spite of the massive size of this tumor, the measurements by the Vastine and Kinney method fall within normal limits (indicated by broken lines), while the proportional method shows the gland to lie posterior to the normal zone (solid lines).

DISCUSSION

In estimating the value of the graphic or proportional method, one must eliminate all lateral shifts from consideration since these two methods involve only measurements of the lateral skull film. For example, temporal tumors more often than not, produce no shift that can be detected by measuring this film, but a lateral shift from the midsagittal plane is present in practically all cases. Our results are summarized, first, comparing the results of the methods and second, a consideration is given to importance of the lateral shift.

Vastine and Kinney reported displacement of the pineal either backward or downward in 25 out of 35 frontal tumors (slightly over two-thirds), and Dyke in 14 out of 26 cases (slightly over one-half) of gliomas and meningiomas. In our series, 18 out of 37 cases were found displaced either backward or downward by the graphic method (approximately one-half). In each of these three series, one case was noted in which the pineal was located either in front of or in front of and above the normal. Only one interpretation can be placed in this finding, namely, that misleading information may be given by this method. Many frontal tumors remain silent or are discovered late. Their bulk is considerable and it would appear unlikely that the pineal could be drawn toward it. Therefore, in the graphic method in nearly one-half the cases, the

position of the pineal was not found to be helpful in localizing and identifying the lesion. The proportional method accomplished two things; it reduced the number of pineals found in the normal zone (Fig. 4), and eliminated the error in those cases showing forward displacement. The number showing significant displacement was thus raised to two-thirds of the cases.

In temporal and parietal tumors, displacement of the pineal was much less frequently noted in the lateral film and invariably noted in the anteroposterior film. The most common direction of displacement was similar to that noted in frontal tumors, either backward or downward (Figs. 5 and 6). Dyke noted the displacements of these types in seven out of 24 temporal tumors. There were two cases in which forward displacement was indicated. Vastine and Kinney noted backward displacement in six out of 15 cases, while in our series by their method, 10 out of 29 cases with temporal tumor were noted either displaced backward or downward.

Displacements are relatively infrequently observed on the lateral film in tumors of the posterior fossa, the floor of the middle fossa, and third ventricle tumors, regardless of the method employed. Localizing information is less often obtained, not only because the measurements fall within normal limits frequently but also because many gliomas occur within the cerebellum at an age period when calcification is not present. The diagnosis in these cases of necessity must rest on other information.

Lateralizing information can be reliably determined only by actual measurement of the anteroposterior and postero-anterior films. Stereoscopic impressions obtained from lateral films are unreliable even if the observer possesses excellent stereoscopic vision. In this series, a lateral shift was often observed in tumors or fluid of the temporal or parietal regions, less often in frontal tumors (over one-half of the cases), and very rarely in sellar or cerebellar tumors. Vastine and Kinney did not determine the relative percentages in this manner but stated that in 23 verified cases of lateral displacement, four were in the frontal lobe, nine in the temporal, six in the parietal lobe, while two showed intracranial hemorrhage. Dyke similarly did not give information concerning the number of pineals identified at midsagittal plane but stated that in 23 cases of gliomas and meningiomas in which there was evidence of lateral displacement, two were found in the frontal, eleven in the temporal, three in the parietal, five in the occipital regions, and one was located subtentorially.

Davis has stated that, in his experience, the Vastine and Kinney method has not aided him in localizing masses within the cerebral lobes. A shift to the right or left of the midline helped in the lateralization of a mass above the tentorium but still failed to identify the lobe involved. This has been the common experience of most workers in this field. In this series, this was true to a large extent. However, certain general rules may prove helpful if the shifts in all the three planes of space are considered.[3]

1. The absence of a lateral shift, determined by actual measurement of the anteroposterior or postero-anterior film, combined with a shift backward or downward, is strong evidence in favor of a frontal tumor.

2. The presence of a lateral shift, combined with normal position in respect to the other two planes of space, is strong evidence in favor of a temporal or parietal tumor or a unilateral collection of fluid of these regions.

3. The absence of a lateral shift practically rules out a space-occupying mass in the temporal lobe and renders a parietal tumor highly unlikely.

4. The absence of any shift in the three planes of space in the presence of a brain tumor indicates usually a subtentorial mass or a basilar midline mass above the tentorium.

5. The presence of a lateral shift combined with marked displacement backward

[3] The assumption is made in drawing up these aids in localization that a space-occupying mass is present.

TABLE I.—OUTLINE FOR AIDING IN LOCALIZATION OF TUMORS

Correlating the type of pineal shift with the possible locations of the tumor within the brain

Lateral Shift	*B* or *D* Shift*	*F* or *U* Shift*	Location of Tumor
0	0	0 or slight	Subtentorial or basilar mass near midline. Rules out temporal and parietal tumors and renders frontal tumors unlikely.
0	+	0	Frontal tumor or basilar midline mass above tentorium. Rules out temporal, parietal, and occipital tumors, also subtentorial masses.
+ (marked)	0	0 or slight	Temporal or parietal tumors, less commonly frontal tumors. Rules out cerebellar tumors.
+	+ (marked)	0	Frontal tumors, also temporal and parietal tumors. Rules out cerebellar tumors.
+ (marked)	0	+	Occipital, less commonly temporal or parietal. Rules out frontal. Renders subtentorial mass unlikely.

* *B*, *D*, *F*, and *U* indicate *backward*, *downward*, *forward*, and *upward*, respectively.

or downward favors a frontal mass but does not exclude a temporal or parietal tumor above the tentorium.

6. The presence of a lateral shift combined with a forward or upward shift in the other plane of space may indicate an occipital mass or a sellar tumor and rarely a temporal or parietal mass.

CONCLUSIONS

1. A comparison of the graphic and proportional methods in 147 verified cases of space-occupying masses within or at the surface of the brain revealed a correct interpretation of the position of the pineal in the higher proportion of cases by the proportional method than by the graphic method.

2. This was particularly apparent in that group of brain tumors (frontal tumors) which commonly give either no or very uncertain localizing signs clinically. In this group diagnostic accuracy in detecting a pineal shift was increased approximately from 50 per cent to 75 per cent.

3. The presence, direction, and character of the pineal shift has been analyzed and correlated with the type and location of the tumor within the brain.

4. By combining the information gained from the anteroposterior film regarding the presence or absence of a lateral pineal shift with the information or data gained from the lateral film by the proportional method, a tentative outline for aiding in the localization of tumors is proposed which may be helpful under the following conditions: (*a*) the pineal is sufficiently calcified to permit its certain identification on both the anteroposterior and lateral films; (*b*) a shift can be identified on either the anteroposterior or lateral skull films or both. This outline, it should be recognized, does not permit localization of all tumors but rather eliminates many regions as possibilities and aids in restricting the latter to a few locations.

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A STUDY OF TISSUE DOSAGE AND RADIATION EFFECT IN CASES OF OPERABLE CANCER OF THE BREAST TREATED BY A COMBINATION OF PRE-OPERATIVE IRRADIATION AND RADICAL MASTECTOMY[1]

By FRANK E. ADAIR, M.D., E. L. FRAZELL, M.D., *and* EDITH H. QUIMBY, M.A., Memorial Hospital, *New York City*

FOR a number of years, various combinations of surgical and radiological methods have been widely used in the treatment of operable breast cancer. Chief of these has been the so-called post-operative prophylactic irradiation after radical mastectomy. During the years 1933–1937, pre-operative irradiation has been employed routinely in operable cases of breast cancer at the Memorial Hospital. This combination of heavy external irradiation with subsequent radical surgery in the operable cases has not been used long enough to warrant evaluation of five-year end-results. It has been demonstrated, however, that this method of therapy results in certain problems of increased morbidity, greater technical operative difficulties, and in a larger percentage of post-operative complications. Some of these clinical problems are reported in detail by one of us (1) in a preliminary report and the subject will not be further discussed in this connection. It is hoped that in time the end-results will show sufficient improvement over those formerly obtained by surgery alone, or surgery and post-operative irradiation, to justify the increased expense to the patient, the greater incidence of complications, and the greater burden on the surgeon and radiologist.

Four years ago, soon after the beginning of this work, it became evident that there was a wide variation in the radiation response of breast tumors of apparently the same clinical type. At operation, it was noted in a few cases that although the tumor had completely disappeared clinically, fully viable cancer cells were identified microscopically in the region of the former tumor, especially in the axillary tissues. In other cases, either no cancer cells could be found, or those cells which were found showed varying degrees of radiation damage such as atrophy, cell hydrops, and sclerosis. These changes were more commonly seen in the primary breast tumor than in the axillary nodes. The studies in this report will cover only a consideration of the breast tissues, and *not* the axillary contents. Cases showing complete microscopic disappearance of the breast tumor showed abnormal tissue changes, which are interpreted by the pathologist as evidence of the pre-existing cancer. Some cases showed residual gross tumor but the cells showed some of the radiation changes above mentioned.

These observations made in the Pathological Laboratory by Dr. Stewart were of sufficient interest to warrant establishing a scale of radiation effect as follows (2):

"R.E.B. — indicates the radiation effect in the breast tumor.

"R.E.N. — indicates the radiation effect in the axillary nodes.

"R.E.B. 0—signifies that irradiation destruction is most incomplete and has been minimal. It may signify that there was a complete destruction in one area with persistence of viable disease in another area.

"R.E.B. 1—signifies the minimum effects of irradiation, such as atrophy, cell hydrops, and slight sclerosis.

"R.E.B. 2—signifies a more marked condition, but similar to R.E.B. 1.

"R.E.B. 3—signifies that the process of tumor tissue destruction has been extremely marked, and that there is a question whether the tumor cells are viable. It will remain for the element of time to prove whether this R.E.B. 3 group is capable of regeneration or metastasis. Dr. Ewing is of the impression that the cases falling into this group may eventually be completely cured and incapable of recurrence. We are taking the position, at least for

[1] Presented before the Fifth International Congress of Radiology, Chicago, September 13–17, 1937.

the present, that this group may be capable of recurrence.

"R.E.B. 4—signifies that after a most careful study has been made of tissues taken from many portions of the breast, there is no sign of cancer."

In many cases the effect of radiation of the tumor was rated as zero, even though a large tumor had clinically disappeared under therapy. This may not mean that profound changes were not present, but that the pathologist has thought wise to be dogmatic in dealing with this point. He reasons that a case showing any unaltered cancer cells at operation, even though 99 per cent of the tumor has clinically disappeared, should be listed as "radiation effect, zero." The analogy to the removal by the surgeon of 99 per cent of the primary tumor is clear, as long as radiosensitivity and radiocurability are not confused.

The effect of radiation in bringing about tumor regression is very incompletely understood. It would, however, seem evident that for the desired reaction to be produced, a certain minimum amount of radiation must be delivered either to the tumor itself, or to tissues immediately surrounding it. Since tumors vary greatly in size, depth, and in the amount of overlying tissue, it is evident that, from the same x-ray beam, very different doses of radiation may be delivered to the deepest lying cells. Obviously, then, the specifications of radiation dosage as a certain number of roentgens, or of milligram-hours per port are entirely insufficient. It is possible for a small superficial mass to receive a much greater dose from 1,000 roentgens per port than a larger, deeply seated tumor from 2,000 roentgens per port. No really worthwhile information regarding the necessary dose of radiation will be available until the actual doses delivered to the tissues in question have been measured, in a large series of cases, and correlated with the observed effect.

From the point of view of the physicist the whole question of tissue dosage is in an unsettled state. No satisfactory unit has been developed, especially for radium radiations. In recent years, physicists have devoted much time and thought to the problem, and it is to be hoped that something practical will soon be available. However, it is not necessary to wait for the perfect physical solution before starting the clinical work. If careful records are kept of the size, shape, depth, and position of the mass and of all the radiation factors, dosage may be specified in terms of any usable unit, and later translated to a new one if desired.

The object of this report is to present a correlation between the amount of radiation actually delivered to the tumor and the radiation effect resulting. When the dimensions and location of the tumor are known, it is possible from available physical data to calculate the minimum dose delivered to the lesion. By correlating these doses with the resultant radiation effects, it should be possible to determine the minimum dose which must be delivered if a satisfactory regression is to be hoped for. Such studies have been published for lesions primary elsewhere in the body (3, 4, 5, and 6). The effect of such factors as age of the patient, and interval between irradiation and operation have also been studied in these groups of cases.

In this report we have calculated the minimum dose delivered within the tumor mass, in two series of cases: one treated by the radium element pack and one by 200 kv. x-rays, and the data, correlated with the resulting radiation effect in the tissues. The size, shape, depth, and position of the primary tumor were carefully determined, examinations being made by at least two clinicians, and many times, by four. The patient was assigned to the radium or x-ray group, as the case might be, and treatment was carried out accordingly. Subsequently, usually from six weeks to three months after irradiation was completed, a radical mastectomy was performed, and the entire breast and axillary contents subjected to careful pathological study.

Every case had been classified as "pri-

mary operable"—in other words, a case offering a good chance of cure, one in which by clinical estimate, the disease had not spread beyond the axilla, and in which no surgery or radiation had previously been employed.

Every case had an aspiration biopsy, which was positive for carcinoma, before the irradiation program was started. The surgical wound of a formal biopsy precludes such a heavy radiation program. Aspiration biopsy tells us that the lesion is cancer, but does not give us many details concerning the type of cancer. (A possible exception is colloid cancer.) Those unfamiliar with the accuracy of this method of biopsy might naturally doubt that cancer had ever been present in the breast, if no cancer cells were found at operation. However, we have verified the aspiration diagnosis of breast tumors in many hundreds of cases during the past six years. Added proof of its accuracy is seen in these cases in which R.E.B. 4 is noted in the breast, but active or atrophic cancer cells are found in the axillary nodes, where, for technical reasons, it is more difficult to deliver a sterilizing dose of radiation.

The doses delivered to the tumors have been calculated in terms of threshold dose (T.E.D.), as ordinarily used at the Memorial Hospital. Up to the present time, this has seemed to us the most practical scheme. It will be possible to translate the doses (approximately) here given into terms of any unit which may later be adopted.

The cases in the radium pack series were treated with the four-gram pack, at a target-skin distance of 6 cm. with a circular field of about 80 square centimeters. In general, the primary lesion was treated first, two ports (an anterior and a lateral) being used, and each receiving a treatment of 8,000 mg.-hr. on alternate days to a total of from 16,000 to 24,000 mg.-hr. per port. The treatment of the primary lesion was thus completed in a week or less. Following this, three axillary ports were treated, one each day (anterior, direct, posterior) to the same total dose, if possible.

In the x-ray series the factors were: 200 kv. (peak), 0.5 mm. copper and 3 mm. aluminum filter, 50 cm. target-skin distance, an intensity of about 60 r per minute, and fields varying from 80 to 250 square centimeters. The treatment of the primary lesion and the axilla were carried out in a single series (instead of completing the one before starting the other). In general, the same five ports were used as above, two to the breast and three to the axilla. Two ports were irradiated daily, with 300 r each (measured in air), to a total of from 1,200 to 2,400 r per port, the entire treatment thus requiring from three to four weeks.

Tissue doses were calculated from isodose curves made with a small "air wall" ionization chamber and water phantom. For the radium pack, the threshold dose at 6 cm. is about 9,000 mg.-hr., so that a case receiving 24,000 mg.-hr. per port received a dose on each skin area of 2.7 T.E.D. The dose in the depth of the tumor is, of course, the sum of the depth doses from the two beams. For x-rays the threshold dose is about 500 r, so that a field receiving 1,800 r had a skin dose of 3.6 T.E.D.

No attempt has been made to calculate the doses for the axilla, possibilities for error here being considerably greater than in the case of the primary breast lesion.

No claim of accuracy is made for the doses arrived at. It is recognized that several factors contribute to error, both in the original measurements of the mass, and in uncertainty as to whether the beam of radiation strikes the tumor exactly as it was intended. However, we do feel that the approximations made are sound, and that worthwhile conclusions may be drawn from the material here presented.

Approximately 300 operable cases of breast cancer have been treated by this method since we began the work in 1933. Many of these were treated since the completion of this report. We have selected 201 case histories, containing sufficient data and details of tumor depth,

shape, and size to permit of the desired calculations. Table I indicates the distribution of cases between the two forms

TABLE I.—RADIATION EFFECTS OBSERVED IN 201 CASES OF CARCINOMA OF THE BREAST TREATED BY PRE-OPERATIVE IRRADIATION

Radiation Effect Breast	Treated by X-rays		Treated by Radium Pack	
	No. Cases	Per Cent	No. Cases	Per Cent
0	54	39	25	40
1	14	10	10	16
2	14	10	4	6
3	26	19	10	16
4	30	22	14	22
Total Cases	138		63	

of radiation therapy, namely, 138 x-ray cases and 63 radium pack cases. The radiation effects are recorded, and graded according to the Stewart scale above quoted. It is thought that grouping together R.E.B. 3 and R.E.B. 4 is justified. Dr. Ewing and Dr. Stewart feel that the R.E.B. 3 cases show such severe radiation damage that they probably will not show a return to activity and will probably go on to complete sterilization. In that event, the end-results as far as radiocurability is concerned, would be the same. In this analysis, the two groups will be placed together with the understanding that they do not represent exactly the same condition, as far as radiation effects are concerned. For purposes of analysis, it was likewise thought best to place together groups R.E.B. 1 and R.E.B. 2. While the changes observed in these groups are varied enough to allow the pathologist to differentiate them, the differences in the changes in either group are not so marked as to preclude their inclusion together for the purposes desired.

It is important to know whether the clinical opinion of degree of regression gives a true picture of the radiation effect obtained. The degree of clinical regression is frequently expressed in rather indefinite terms, which are, therefore, of relative value only. For purposes of analysis it was necessary to assign some sort of

TABLE II

Clinical regression	Grade 0:	Increase in size of tumor; or no change.
" "	Grade 1:	Slight decrease in size of tumor.
" "	Grade 2:	"Considerable decrease;" "Marked decrease;" "Residual thickening only."
" "	Grade 3:	Complete clinical disappearance of tumor.

TABLE III.—COMPARISON BETWEEN RADIATION EFFECT AND CLINICAL REGRESSION OF BREAST CANCERS

Clinical Regression	Total No. Cases	R.E. 0		R.E. 1 and 2		R.E. 3 and 4	
		No.	Per Cent	No.	Per Cent	No.	Per Cent
X-rays							
0	9	7	78	2	22	0	0
1	22	15	68	5	23	2	9
2	30	13	43	10	33	7	24
3	56	10	18	6	11	40	71
Radium							
0	2	2	100	0	0	0	0
1	5	3	60	2	40	0	0
2	14	6	43	7	50	1	7
3	28	6	21	1	4	21	75

arbitrary rating for these terms if they were to be of comparative value. In Table II will be found the one agreed upon.

In Table III we have compared the degree of clinical regression with the microscopic radiation effect observed by the pathologist, for all cases in which a statement of clinical opinion was found on the history. It is seen that some tumors had completely disappeared clinically which were rated by the pathologist as showing no radiation effect (R.E.B. 0); there were actually 10 such cases in the series of 56 R.E.B. 0 cases, or 18 per cent. It is probable that the residual disease was obscured by edema of the surrounding tissues, or by fibrosis and infiltration incidental to irradiation. Areas of mastitis in the breast also increase the chance of error in clinical impression. There is also the possibility that the fully viable and unaltered cancer cells found in the breast were manifestations of renewed activity of the tumor, but this is extremely unlikely.

A high percentage of the cases which showed little or no clinical regression showed R.E.B. 0, and those cases showing apparent complete clinical regression usually demonstrated marked destructive effect on the cancer. In general, therefore, it may be stated that the greater the clinical regression, the more likely the tumor is to show a high radiation effect. *Of the x-ray and radium cases 71 per cent and 75 per cent, respectively, which were stated to show complete regression, showed either complete microscopic absence of cancer cells, or else only a few scattered and badly damaged ones.* Hence, we feel that the clinical impression can be fairly well relied on to follow the scale of radiation effects. We may state that in approximately three out of four cases which show complete clinical regression, the radiation effect in the tumor will be profound.

This study naturally leads to a consideration of the amount of effective radiation delivered to tumors (T.E.D.) showing varying grades of clinical regression. In Table IV the dose of radiation (T.E.D.) is compared with the amount of clinical regression. For purposes of analysis, cases were grouped as to whether the calculated effective tumor dose was less than, or greater than, 4 T.E.D. in the x-ray group; and less than, or greater than, 1.5 T.E.D. for the radium group. The figures would indicate that, as is to be expected, the percentage of cases showing the advanced stages of clinical tumor disappearance increases as the higher calculated tumor doses are reached. For example, in the x-ray group 34 per cent of the cases with a calculated tumor dose of *less* than 4 T.E.D. showed "clinical regression Grade 3," whereas 57 per cent of the group with calculated dose of *greater* than 4 T.E.D. showed the same amount of advanced clinical regression. In other words, of the 58 cases receiving x-ray therapy, 57 per cent of the tumors clinically disappeared *if* they received *more* than 4 T.E.D.; while only 34 per cent of the tumors clinically disappeared if *less* than 4 T.E.D. were given.

TABLE IV.—COMPARISON BETWEEN CLINICAL REGRESSION AND THRESHOLD DOSES

T.E.D.	Total No. Cases	Clinical Regression							
		0		1		2		3	
		No.	Per Cent	No.	Per Cent	No.	Per Cent	No.	Per Cent
X-rays									
Less Than 4	58	12	21	17	29	10	17	20	34
Greater Than 4	58	7	12	12	21	6	10	33	57
Radium									
Less Than 1.5	21	2	10	6	29	2	10	11	52
Greater Than 1.5	28	2	7	2	7	1	4	23	83

TABLE V.—RELATION BETWEEN TUMOR DOSE AND RADIATION EFFECT

X-rays

Tumor Dose (T.E.D.)	Total No. Cases	Radiation Effect					
		R.E. 0		R.E. 1 and 2		R.E. 3 and 4	
		No.	Per Cent	No.	Per Cent	No.	Per Cent
Less Than 2	9	6	67	0	0	3	33
2–4	68	29	43	18	26	21	31
4–6	45	16	36	8	27	21	47
More Than 6	16	3	18	2	13	11	69
Radium							
Less Than 1	8	2	25	5	63	1	12
1–2	46	21	46	7	15	18	39
2–3	9	2	22	2	22	5	56

More accurate data for comparison than the clinical regression are to be found in the relationship existing between the microscopic radiation effect and the calculated effective dose (T.E.D.) delivered. For example, in Table V we see that in the x-ray group, the percentage of R.E.B. 0 cases falls (67 per cent–18 per cent) as the calculated tumor dose increases. At the same time, the percentage of R.E.B. 3 and R.E.B. 4 cases rises (33 per cent–69 per cent) as the tumor dose increases. Such data confirm the usual statement that *the larger the minimum dose delivered to the tumor, the more likely is its radiation effect to fall in the higher groups*. It might be pointed out that doses in excess of 6 T.E.D. are desirable, since 69 per cent of the cases receiving this dose showed a radiation effect of R.E.B. 3 or R.E.B. 4.

It is obvious that in any particular case there is a definite relationship between the amount of radiation falling on the skin and the amount of effective radiation reaching the tumor. It would seem apparent that the larger the skin dose, the larger will be the effective radiation dose received by the tumor. But, since the tumors are situated at different depths, this does not always hold true, and it must be pointed out that expressions of dosage per skin portal are insufficient for clinical reports. Reference to any set of depth dose curves will make this point obvious. Attention has already been called to the fact that a tumor situated close to the skin surface can receive a larger effective tumor dose from a comparatively small dose on the skin than a tumor much more deeply placed and receiving a much larger dose on the skin.

In Table VI we have tabulated the cases according to the dose of radiation falling on the skin, with their calculated minimum effective tumor dose. In the x-ray group the majority of the cases received greater than 1,800 r per skin portal; in the radium

TABLE VI.—RELATION BETWEEN SKIN DOSE AND TUMOR DOSE

X-rays

Skin Dose in r	Total No. Cases	Minimum Tumor Dose in Terms of T.E.D.			
		Less Than 4 T.E.D.		Greater Than 4 T.E.D.	
		No.	Per Cent	No.	Per Cent
Less Than 1,800 r	62	48	78	14	22
More Than 1,800 r	76	25	33	51	67
Radium Pack					
Less Than 25,000 mg.-hr.	44	18	1	26	59
More Than 25,000 mg.-hr.	19	6	32	13	68

group the majority of the cases received less than 25,000 mg.-hr. per portal. Of the cases receiving less than 1,800 r per skin portal, 22 per cent showed a calculated tumor dose of greater than 4 T.E.D.; while 67 per cent receiving *greater* than 1,800 r per skin portal showed the same calculated tumor dose (greater than 4 T.E.D.). This point may be more clearly brought out if two of the x-ray dosage groups, *viz.*, the smaller and the larger, are contrasted (Table VII). Cases receiving 1,600 r on the skin showed almost twice the percentage (62 per cent) with a calculated dose of less than 4 T.E.D. when compared with those greater than 4 T.E.D. (38 per cent). But when the dose on the skin is increased by 50 per cent (800 r) to 2,400 r, we find that the percentage of cases receiving a calculated minimum effective tumor dose of more than 4 T.E.D. is almost four times the percentage (79 per cent) receiving less than 4 T.E.D. (215). It is to be noted that 21 per cent of the cases of the 2,400 r group received less than 4 T.E.D. and 38 per cent of the 1,600 r group showed a calculated tumor dose of more than 4 T.E.D. This emphasizes the fact that expressions of dosage per skin portal are insufficient to convey an accurate idea of the effective radiation delivered to any tumor. Analysis of the radium pack cases, in general, bears out this statement, but the number of cases is too small for statistical analysis.

TABLE VII.—RELATION BETWEEN SKIN DOSE AND TUMOR DOSE

Skin Dose	Total No. Cases	Tumor Dose			
		Less Than 4 T.E.D.		Greater Than 4 T.E.D.	
		No.	Per Cent	No.	Per Cent
1,600 r	26	16	62	10	38
2,400 r	29	6	21	23	79

An important factor in planning irradiation therapy is *the size of the tumor*. The larger the tumor and the deeper its posterior portion from the skin, the smaller the minimum effective dose of radiation which can be delivered to it. In addition, the larger the tumor, the more likely are portions of it to lie off the center of the radiation beam. Since the percentage depth dose is appreciably less at the edges of the irradiated field than near its center, there is more likelihood that peripheral portions of the large tumors will be underdosed. In Table VII tumors of different sizes have been compared with their radiation effects. The grouping of tumors as to size is arbitrary. The limitations of the value of tumor size measurements of the clinician has been mentioned. However, we have grouped them as *small* tumors, if they were estimated to be 4 cm. or less in diameter, and as large tumors if they were estimated to be larger than 4 cm. Table VIII shows that the percentage of profound radiation effects is higher (64 per cent) for small tumors, and lower (46 per cent) for the large tumors.

Since there is such a close relationship between the size of the tumor and the radiation effect obtained, it follows naturally that a comparison of the *calculated minimum effective tumor doses with the size of the tumors* will show a similar relationship. Table IX shows such a comparison. It is natural that this should be true, since it has been shown that the radiation effect on the tumor is directly related to the dosage received by it (see Table V). Thus,

TABLE VIII.—RELATION BETWEEN SIZE OF TUMOR AND RADIATION EFFECT

X-rays

Radiation Effect	No. Cases	Per Cent Total	Size of Tumor			
			Small		Large	
			No.	Per Cent	No.	Per Cent
0	54	39	23	43	31	57
1 and 2	28	20	13	46	15	54
3 and 4	56	40	36	64	20	46
Radium						
0	25	40	12	49	13	51
1 and 2	14	22	8	57	6	43
3 and 4	24	38	11	49	13	51

with the group of small tumors a larger percentage of them received a large dose than received a small dose. The reverse of this condition is seen when large tumors are studied.

TABLE IX.—RELATION BETWEEN T.E.D. AND SIZE OF TUMOR

X-rays

Tumor Size	Total No. Cases	Threshold Doses			
		Less Than 4 T.E.D.		Greater Than 4 T.E.D.	
		No.	Per Cent	No.	Per Cent
Small	59	27	46	32	54
Large	79	46	58	33	42
Radium					
Small	26	5	19	21	81
Large	37	19	51	18	49

A question arose as to whether the radiation effects observed might bear some *relationship to the age of the patient.* The ages varied from 30 to 78 years. However, the percentage of the young and old with radiosensitive tumors was approximately the same. Apparently the poor prognosis in cancer of the breast in young individuals is not due to differences in tumor radiosensitivity.

It has been argued by some that many of the cases showing advanced degrees of radiation effects might eventually go on to complete sterilization if not operated upon. In this group of cases the time interval between completion of treatment and the operation varied from 6 to 416 days. However, the percentage of cases falling into the various radiation effect groups did not vary widely in any of the groups; therefore the time element necessary for sterilization of the tumor seems to be of less importance than was anticipated.

In calculating these doses, no attention was paid to the time factor in irradiation time, or the accumulation effect. Since in either series all cases were treated in approximately the same time, they are directly comparable in themselves. However, before comparing the radium and x-ray results, it is necessary to consider the time factor. With the radium pack, the entire treatment to the primary lesion was administered in six days or less, to any one field in five days or less, and each individual dose was 90 per cent of the threshold dose. With the x-rays, the entire treatment consumed on an average of 21 days, and the dose to any given field usually about 18 days, each individual dose being about 60 per cent of the threshold.

One of us, with Dr. MacComb, has made an extensive study of the recuperation of human skin under roentgen and gamma radiation (see Fig. 1) or the accumulation of radiation effect therein (7 and 8). While our work was, of necessity, limited to mild reactions, it offers very suggestive information in irradiations of the type under consideration in this report. The figure shows the relative recuperation in the skin in any given field, from the two types of therapy used. The total cumulative dose from 24,000 mg.-hr. of gamma radiation is 1.6 threshold dose; that from 1,800 roentgens is 1.4 threshold dose. In other words, although the total dose from the radium was 2.7 threshold doses, and from the x-rays 3.6, actually because of the time factor (or the spreading out of the x-rays over many more days) the cumulative dose in the skin is 15 per cent more from the radium than from the x-rays. The clinical findings bear this out. No serious and permanent skin damage resulted from x-ray therapy, while this was not infrequently observed from radium.

With regard to accumulation in the tumor, no information is available. The whole underlying reason for divided doses rests on the assumption that recuperation is less in tumor cells than in normal ones. In this case, recuperation must be less in tumor cells than in the skin. Whether recovery from the effect of radium and of x-rays proceeds at the same rate is also unknown. In the skin the rate for radium is somewhat less than for x-rays, and the clinical impression is that this is also applicable to the tumor. In any case, it is

evident that, in tumor no less than in skin, it is impossible to make a comparison of the radiation effect of radium and x-radiation on the basis of total dose alone.

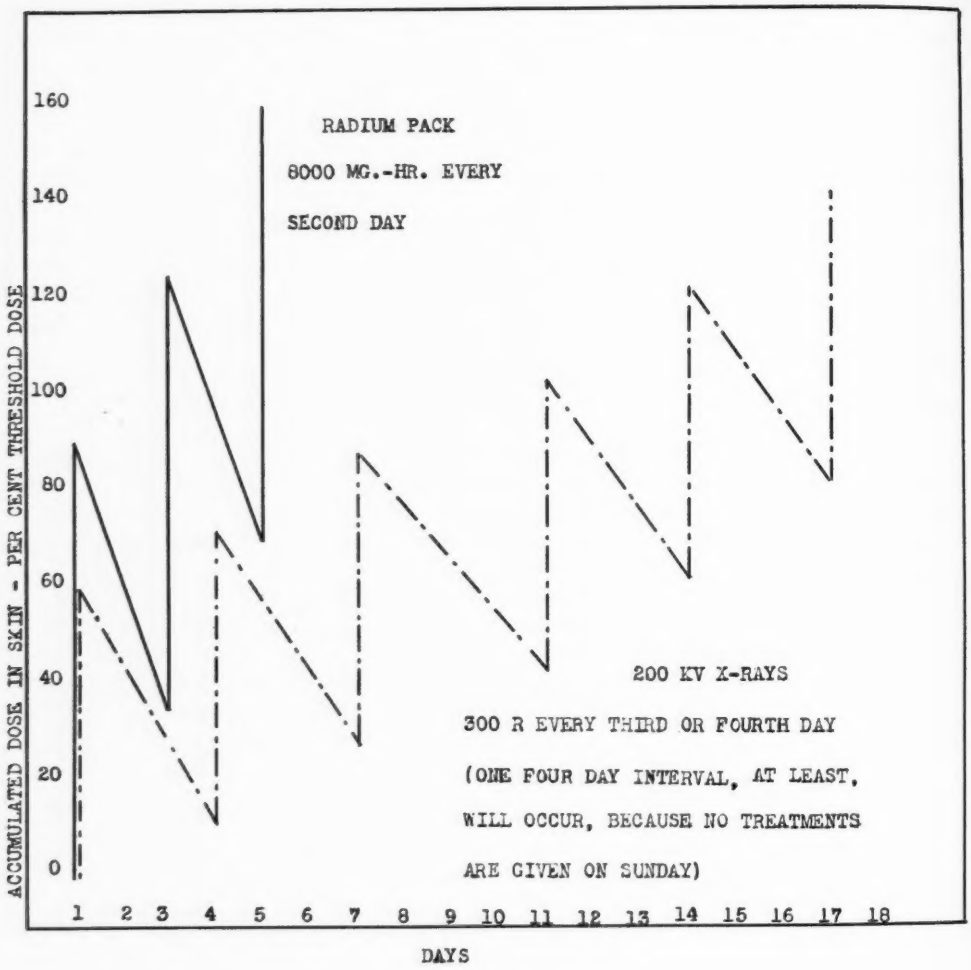

Fig. 1.

These facts must be borne in mind in considering the data submitted. Whereas on the basis of total radiation administered, the radium appears considerably more efficacious in producing tumor regression, on the basis of the *cumulative* dose, such an advantage of radium is not apparent.

SUMMARY

A series of 201 cases of primary operable mammary cancer were subjected to preoperative irradiation, of varying amounts: 138 cases were treated by the 200 kv. x-rays, and 63 cases by the 4-gram radium element pack. After approximately from eight to ten weeks following completion of the preoperative irradiation, a radical mastectomy was performed. The tissues were then subjected to meticulous pathological study.

Before treatment was initiated, careful measurements had been made relating to the exact tumor size, thickness, depth, and position in the breast. With all the physical factors of radiation treatment at hand, a study was then made, correlating the tumor dose (T.E.D.) with the resultant radiation effect in the tumor.

Differing radiation effects are grouped according to a scale of microscopic changes. In both the series treated by x-rays and that treated by the radium pack, certain facts were apparent:

1. The clinical impression as to the residual tumor can be fairly well relied on (71 per cent for x-ray cases and 75 per cent for radium pack cases) to express the radiation effect obtained.

2. The larger the minimum tissue dose delivered to the tumor, the more likely is a profound radiation effect to be obtained.

3. It is necessary to deliver by x-rays at least six threshold skin doses within three weeks, and with radium almost three threshold skin doses within six days to the deepest portion of the tumor, if the maximum radiation effects are to be obtained in 70 per cent and 56 per cent, respectively.

4. There is a definite relationship between the size of the tumor mass and the radiation effect obtained.

5. The chance of obtaining a high radiation effect decreases as the size of the tumor increases.

6. Since tumors vary enormously in size, as well as the *amount* of overlying tissue, it is evident that from the *same* beam of irradiation, very different doses may be delivered to the most deep-lying tumor cells. The inadequacy of expressing radiation dosage as a certain number of roentgens, or of milligram-hours per port, is evident.

7. The age of the patient and the differences in interval between completion of irradiation and operation had no apparent influence on the radiation effect observed in the tumor in this series of cases.

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PRACTICAL ASPECTS OF CALCIFICATION AND OSSIFICATION IN THE VARIOUS BODY TISSUES

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THE recent unfolding of many new facts concerning the mechanisms of calcification, with the concomitant descriptions of new syndromes such as hyperparathyroidism and hypervitaminosis, makes the consideration of the entity, "Calcification and Ossification in the Various Body Tissues," a subject of signal interest to the roentgenologist (1, 2, 3). It is not generally appreciated that there are numerous factors governing calcification, and almost as many theories of the mechanism involved have been propounded.

Fig. 1.

Fig. 2.

Fig. 1. Decalcification of the lumbar spine and bones of the pelvis and several calculi in the left kidney, the result of hypercalcemia in hyperparathyroidism with metastatic calcification in the kidney.

Fig. 2. The entire left kidney and ureter, up to the cystic opening, show fine granular calcification outlining the entire kidney and ureter. This granular calcification resembles the healed miliary tuberculosis in the lungs and here it also represents calcification of miliary tubercles.

FACTORS CONCERNED IN CALCIFICATION

The following brief discussion of the most important factors is of special importance in understanding pathologic calcification in the various tissues (4).

(*A*) *Blood Plasma Calcium.*—A large part of the calcium in the diet must be brought into solution before absorption. This is dependent upon several factors. The soluble salts are thrown out of solution by (*a*) the alkaline carbonates in the digestive juices; (*b*) by fatty acids. The dependence of calcium metabolism upon a normal fat metabolism explains the abnormally low blood calcium values and also the poor absorption of vitamin D, resulting in the bone changes we see in the so-called celiac rickets. Again, acidity of the intestinal contents favors the increased absorption of calcium, otherwise excess phosphorus must be balanced with that of calcium, or excess phosphorus combines with calcium as the insoluble calcium phosphate and causes calcium deprivation.

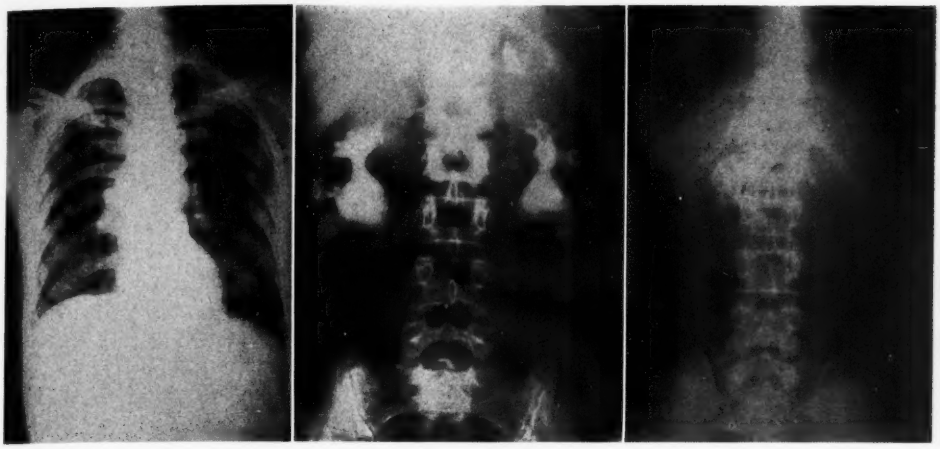

Fig. 3. Fig. 4. Fig. 5.

Fig. 3. Discrete calcified shadows uniformly distributed throughout both lungs with an old healed lesion in the right apex. The calcified shadows represent healing of a miliary tuberculous dissemination in both lungs.

Fig. 4. Two triangular calcified shadows in the region of the adrenals. Intravenous study shows both kidneys, well outlined, with slightly dilated pelves, but with normal calices. The calcified shadows are due to calcification occurring as a result of tuberculosis (Addison's disease).

Fig. 5. Irregular calcified shadows surrounding the bodies of the first and second lumbar vertebræ, as a result of calcification in a cold abscess due to tuberculosis, the tuberculous process in the bodies of the vertebra having cleared up and the abscess entirely calcified.

If calcium is in excess, a certain amount forms the insoluble phosphate and a considerable amount is excreted as other salts.

The excretion of calcium occurs through the kidney and large bowel. So we see the formation of calculi due to excessive excretion of calcium, through the kidney, from over-absorption due, in turn, to acid bowel content. Again, renal calculi are observed in certain bedridden patients, in cases in which decalcification often is due to inactivity, leading to the abnormal excretion of calcium, with deposition. The calculi may disappear when the patient resumes active life.

(*B*) *Vitamin D.*—Vitamin D is essential to normal calcium and phosphorus metabolism. It is indispensable for maintaining the normal calcium and phosphorus concentration and ratio in the blood and for the normal formation of bone. There is an increased net retention of calcium and phosphorus brought about through the resultant of two opposing factors: (1) The increased absorption from the diminished excretion into the intestines; (2) the increased elimination by the kidneys (5, 6, 7).

Hypervitaminosis D can cause widespread calcification in the arteries and possibly in other tissues (8). In children, we have seen hypervitaminosis D cause an unusually dense zone of calcification in the metaphyses of the long bones.

(*C*) *Parathormone.*—The physiological effects of the parathyroid hormone have been briefly outlined by Aub (9):

(1) To raise the blood calcium and lower the blood phosphorus.
(2) Possibly to increase the ionized calcium in the blood.
(3) To increase the calcium and phosphorus excretion in the urine.
(4) To obtain calcium for this increased demand either from a large amount of ingested calcium or from the stores in bones with the mechanism still not definite.

We have all seen the bone changes of hyperparathyroidism.

(*D*) *Other Ductless Gland Secretions.*—The effect of some of the other ductless

Fig. 6.

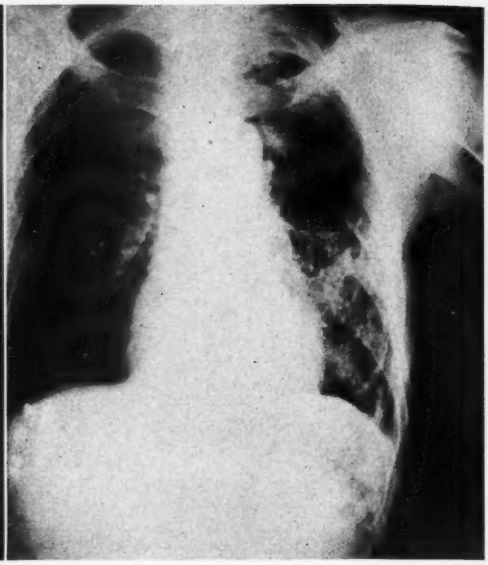

Fig. 7.

Fig. 6. Extensive calcification of the superficial and deep cervical glands, axillary glands occurring in glandular tuberculosis of the bovine type. Other films, not shown here, also demonstrate extensive calcification of the abdominal glands.

Fig. 7. Irregular blotchy calcification in lower half of left lung, occurring in the pleura as a result of an old empyema with calcification of the empyema wall.

Fig. 8-*A*.

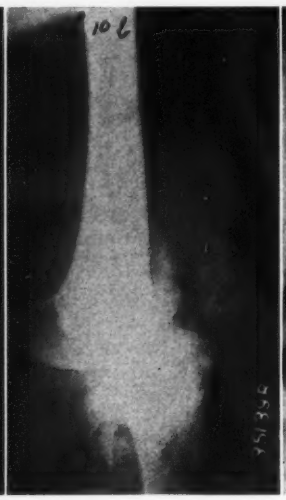

Fig. 8-*B*.

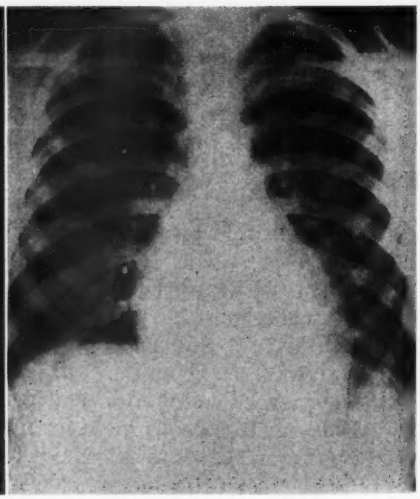

Fig. 9.

Figs. 8-*A* and 8-*B*. Irregular areas of calcification in the soft structures surrounding the articulating portions of the bones of the right knee as a result of a primary osteogenic sarcoma.

Fig. 9. Nodular areas of calcification in both lungs and hilar regions as a result of metastatic osteogenic sarcoma, the primary lesion being in the right hip.

glands on calcium metabolism, though less marked, is definite. Thyroid extract produces an increased excretion of calcium (9, 10), *e.g.*, rarefaction of bones has been ob-

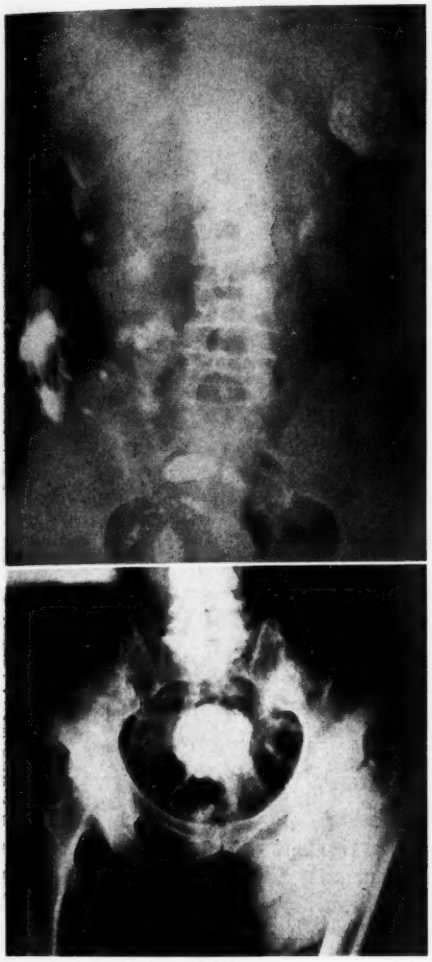

Fig. 10 (*above*). The lower half of the spleen covered with an irregular, mottled, calcified shadow, the result of metastatic malignancy in the spleen, the primary lesion being in the cardiac end of the stomach.

Fig. 11 (*below*). Large, circular, calcified shadow showing stippling in the center. Calcified fibro-adenoma of the uterus.

served in exophthalmic goiter (10, 12), and calcium excretion is increased in exophthalmic goiter after administration of desiccated thyroid (9).

The thymus (13, 14) and the sex glands (15, 16, 17, 18) apparently take some part in calcium metabolism but the influence of the spleen, posterior lobe of the pituitary, and the adrenal gland is still not definitely established (2).

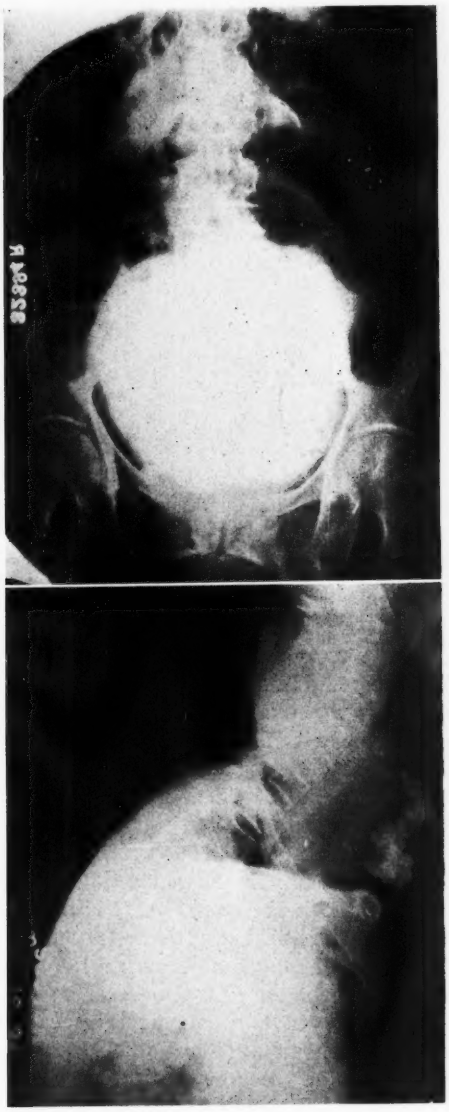

Fig. 12 (*above*). Large, solid ovoid tumor mass, uniform in outline, filling the entire pelvis (lithopedion), due to death and calcification of a fetus.

Fig. 13 (*below*). Dense, irregular calcified shadows in a cystic goiter present for 20 years and recently undergoing malignant changes.

(*E*) *Hydrogen Ion Concentration.*—The concentration of hydrogen ions in a given tissue may be an important factor controlling the deposition of calcium in that an alkaline reaction favors calcium deposition.

Fig. 14.

Fig. 15.

Fig. 16.

Fig. 14. Retrograde pyelogram showing normally outlined pelvis and calices in the right kidney, and in the periphery of the inner and upper portions of the left kidney, dense linear calcification representing a cortical adrenal tumor portions of which have undergone necrosis followed by calcification.

Fig. 15. Several large circular calcified shadows, somewhat separated from one another, showing mottled, small, calcified shadows in the centers. Calcified echinococcic cysts in the liver.

Fig. 16. Small ovoid calcified shadows, about 1 × 3 mm. in diameter, in the muscles of the back and thighs. These calcified shadows run parallel to the long axis of the muscles and represent calcified *Cysticercus* parasites.

The frequency of calcium deposits in the alveoli of the lungs, the uriniferous tubules and the gastric gland areas which possess a slightly alkaline reaction because of eliminations of acid at these points, has been cited as evidence (19).

(*F*) *Phosphatase.*—The enzyme phosphatase, apparently plays a major rôle as a catalyst and is present in particularly high concentrations in the growing portions of the bones of young animals (20). It apparently acts on phosphoric acid esters reaching the tissues, causing the local liberation of phosphate ions and the resultant deposition of calcium phosphate. Phosphatase is increased not only in growing children but also in disease in cases in which extensive decalcification occurs, such as Paget's disease, osteomalacia, and rickets. With improvement, the phosphatase returns to normal.

(*G*) *Blood Supply.*—Leriche and Policard (21) hold that there is a very important relationship between vascularity and calcification of bone, since the process of halisteresis is stimulated and accelerated by an increase in arterial blood. As a result, we see decalcification of the bone with hyperemia of the area and osteosclerosis, if there is anemia of the diseased part.

METASTATIC CALCIFICATION

This is a condition of deposition of lime salts in tissues with increase of plasma calcium, usually due to some generalized rarefying disease of bone, and was first described by Virchow in 1855 (22). Nephritis is often present and may be of importance in causing a retention of calcium of the blood, but it is not invariably present. The causes of bone resorption which may give rise to metastatic calcification are many: Tumors, *e.g.*, sarcoma and carcinoma of bone (23, 24, 25), multiple myeloma (26), myelogenous leukemia (27, 4), osteosarcoma and caries of the spine (28, 29), hyperparathyroidism (Fig. 1), and Albers-Schönberg disease. The significance of nephritis as a concomitant factor in the production of this condition has been emphasized by several writers and those cases in which nephritis was unassociated with other obvious changes demonstrate its importance (32, 33).

The experimental deposition of calcium by intravenous or intraperitoneal injection, at a distance from the site of introduction, has also been obtained (34). It has also been produced by the addition of acid to the diet, possibly by causing increased absorption of calcium. Experimental administration of parathyroid hormone and of toxic doses of irradiated ergosterol have also given rise to calcium deposits (35, 36). In these last experiments, the distribution of the calcium is similar to that occurring in disease, in cases in which the direct injection of calcium gives rise to an unusual distribution.

Fig. 17.

Fig. 18.

Fig. 17. Irregular dense calcified shadow, 2 × 3 cm. in diameter, in the right frontal region due to a tuberculoma in the brain.

Fig. 18. Many nodular calcified shadows, ranging from 3 mm. to 1 cm. in diameter, distributed in the brain. These shadows are present in the meninges and represent healed tuberculous lesions.

Fig. 19-*A*.

Fig. 19-*B*.

Fig. 19-*A*. Postero-anterior view. Extensive calcification in the aorta and a calcified oval shadow which is in the heart mass, above the diaphragm, typifying calcification in the aortic ring.

Fig. 19-*B*. Left oblique view. Extensive calcification and tortuosity of the aorta and the calcified oval aortic ring in the posterior portion of the heart is shown to better advantage.

DYSTROPHIC CALCIFICATION

When the organism has a portion of dead

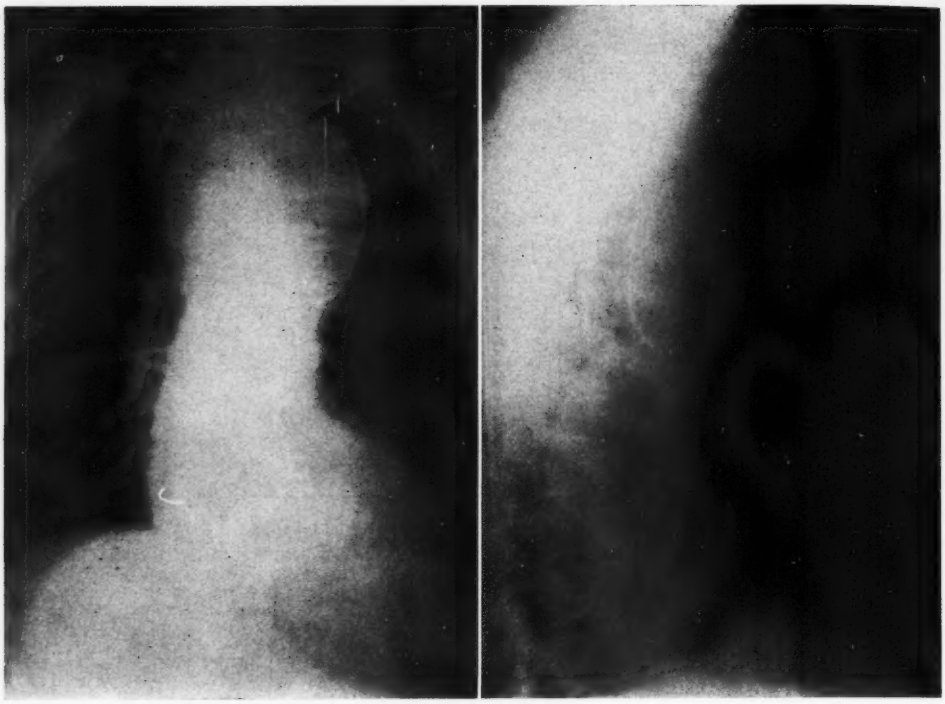

Fig. 20-*A*. Fig. 20-*B*.

Fig. 20-*A*. Postero-anterior view. Large saccular aneurysm with dense linear calcification in the sac, displacing the trachea to the right. The heart is not enlarged.

Fig. 20-*B*. Lateral view. Showing the origin of the aneurysm from the mid-portion of the arch, the remaining portion of the aorta being normal. There is some erosion of the anterior surface of the dorsal vertebra.

tissue that does not suppurate, it usually becomes infiltrated with lime salts. Besides the totally necrotic areas, the most frequently calcified areas are the masses of scar tissue that have become hyaline subsequent to impaired circulation by contraction of the tissue around the vessels. This form of calcification is often called "dystrophic calcification." Probably the only exception to the rule that the tissue must be dead or dying before calcification occurs is in metastatic calcification.

This form of calcification is most commonly seen in chronic tuberculous lesions (Figs. 2, 3, 4, 5, 6), in the lining of chronic empyema cavities, (Fig. 7), and in various tumors, both primary (Fig. 8), and secondary (Figs. 9, 10). The fibro-adenoma (Fig. 11) of the uterus, lithopedium (Fig. 12), the adenoma of the thyroid (Fig. 13), the hypernephroma (Fig. 14), and other kidney tumors are relatively frequent sites of pathologic calcification. Calcified parasites, while infrequent, cannot be dismissed by mere mention. Calcification in the following organisms have been found by us: The echinococcus (Fig. 15), cysticercus cellulosæ (Fig. 16), and trichina spiralis.

The echinococcus cysts are larger than any of the other parasitic lesions. Calcification usually starts in the outer wall as irregular plaques over a curved surface. Finally the entire cyst may shrink and calcify. The cysticercus calcification appears as a multiple ovoid. Shadows, three-tenths to one centimeter in length, are scattered in the muscles, with their long axis in the principal axis of the body. The calcified *Trichina* parasite is somewhat

smaller than the *Cysticercus*, being usually the size of a grain of sand and is difficult to see with the naked eye.

and in which they may present a serious diagnostic problem. The cranial cavity is such a structure (38). Normally, one

Fig. 21-*A*. Fig. 21-*B*.

Figs. 21-*A* and 21-*B*. Calcified long sapenous vein. The denser calcified shadows are in the valves of the veins and the calcification is not uniform, as in the arteries.

Calcification in tendons, particularly in the tendon of the supraspinatus muscle, and in the various bursæ, is a very frequent finding. In the shoulder, the calcium deposit is usually in the supraspinatus tendon and, due to its close proximity to the subachromial or subdeltoid bursa, the diagnosis of a calcified bursitis is usually made (37). The shadow may vary from a few millimeters to several centimeters in diameter. The amorphous carbonates and phosphates form a liquid mass between the fibers of the tendon with no capsule or limiting membrane.

A common site of ossification is in the achilles tendon, especially after injury. This is also seen in the joint capsules, particularly in the femur.

There are certain parts of the body in which calcified areas are commonly seen may see calcification occurring in the pineal gland and choroid plexus, the falx cerebri, and in the tentorium, particularly about the sella turcica, especially in that portion connecting the posterior clinoids with the petrous ridges. Usually, calcification in any other area within the skull suggests a tumor. Rarely, tuberculosis (Fig. 17) as a single lesion or even multiple tuberculomas (Fig. 18) may be noted. The pineal gland is calcified in approximately 50 per cent of cases. Calcification occurs less frequently in the choroid plexus than it does in the pineal gland. A similar punctate type of calcification occurs in psammomas but the opacities in psammomas are larger and more numerous and the situation is different. The calcifications in the falx are most often seen as oblong or irregular opacities: they are never round and there

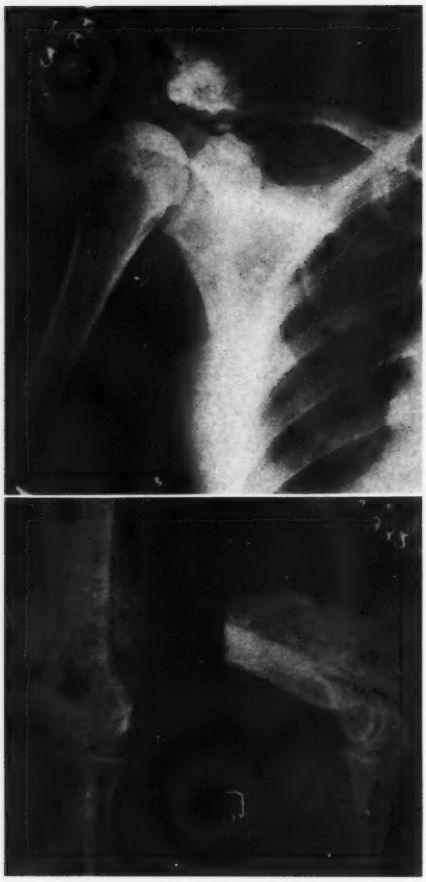

Fig. 22-*A* (*above*). Calcinosis circumscripta. Large irregular globular calcification near the right acromioclavicular articulation.

Fig. 22-*B* (*below*). Case similar to that shown in Figure 22-*A*. Dense amorphous calcification in the muscles and fascia of the lower half of the humerus.

may be one in each side of the superior longitudinal sinus. Irregular calcification takes place in many meningiomas but they are never as large as calcifications in the falx; they are always multiple and tend to assume a round or oval shape. The extensive new bone formation with spicule development, so characteristic of meningiomas, is due to a bone reaction and must be distinguished from calcifications in the tumor itself. Somewhat similar calcification to that in ependymomas occurs in solitary tubercules but, according to Camp (39), calcification in tubercles is compact and dense and this is not the case in ependymomas.

From 70 to 80 per cent of suprasellar cysts show calcification in their walls, a most important point to remember when treatment of a pituitary lesion is under consideration. A circular line of calcium above the sella is diagnostic of suprasellar cyst. In the same region one finds semilunar areas of calcification due to atheromatous plaques in diseased and aneurysmal carotid arteries. A patient with a cerebral abscess rarely lives long enough for calcification to take place in the walls of the abscess. Should he survive, calcification appears in thin round opacities similar to those seen in suprasellar cysts.

Much is now being written about calcification in the heart and blood vessels. Intracardiac calcification is most often seen in the aortic (Fig. 19) and mitral valves and in the left annulus fibrosus. The tricuspid and pulmonary valves and right annulus fibrosus are rarely affected. The calcifications are multiple usually semilunar or sabre-shaped, and can be distinguished from calcified costal cartilage or sternum (*a*) by their position in the heart shadow, (*b*) by characteristic dancing movement on the fluoroscopic screen. Bishop and Roesler (40) state that calcification of the aortic valve may be associated with calcified infarcts in the kidneys, hyperostosis of the frontal bone, and calcification of the nucleus pulposus of the intervertebral disks. Irregular calcification of the endocardium is sometimes seen in cases of subaortic stenosis.

Calcification of the myocardium is well known and is visualized radiologically in myocardial degeneration and infarct following coronary thrombosis. It has been described in cases of chronic sepsis and renal disease and in association with osteitis fibrosa cystica. Actual plaques in the coronary arteries have been demonstrated as linear, segmental, and curved shadows corresponding to the course of arteries.

Calcified plaques, the result of arteriosclerosis, occur very often in the walls of

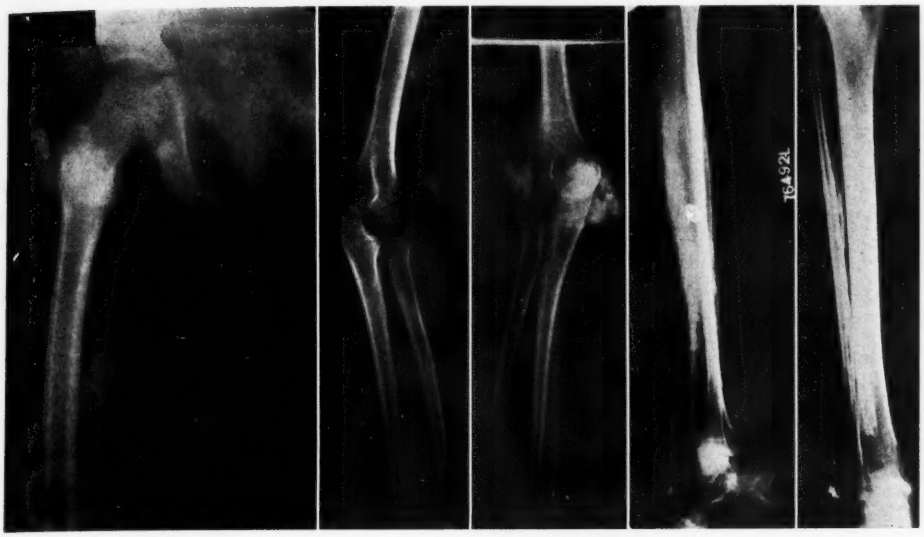

Fig. 23-*A*. Fig. 23-*B*. Fig. 24.

Fig. 23-*A*. Calcinosis universalus. Irregular calcified areas in the fascia, muscles, and subcutaneous tissues of the thigh, separated from the bone and running parallel to the soft structures of the leg.
Fig. 23-*B*. Irregular calcification in the fascia and muscles around the elbow and arms.
Fig. 24. Myositis ossificans, showing layers of ossified bone in the muscles of the left lower leg, separated from the shaft but running parallel to it.

the aorta, especially in the region of the knob, and in the lower abdominal portion. These plaques are a very common finding in the lower extremities, particularly in diabetic patients. The walls of aneurysms (Fig. 20, *A* and *B*) very frequently show calcification in the sac. Phleboliths frequently form in the pelvis (Fig. 21), with the veins showing a solid ossification with rounded dense areas near the valves.

CALCINOSIS

Calcinosis may be defined as the abnormal deposition of calcium salts in the skin, subcutaneous tissues, muscles, and the tendons of the body (41). It may be subdivided into two general groups—calcinosis circumscripta and calcinosis universalis. In calcinosis circumscripta (Fig. 22), the calcific deposits are primarily limited to the extremities and their deposition is frequently symmetrical. The deposits of calcium are often found around the joints. The condition is most prevalent in persons in the second half of life. In calcinosis universalis, there is a tendency for widespread multiple calcareous deposits not only in the skin but in the deeper structures (subcutaneous tissues, muscles, and tendons) especially in the region around the joints. Calcinosis universalis (Fig. 23) is observed in patients in the younger age groups, most frequently in the first two decades of life. The pathogenesis is as yet undertermined. The blood calcium in practically every case of both types has been normal. The condition may be related to dermatomyositis and scleroderma. Roentgen examination may make the diagnosis in cases in which nodules are not palpable by physical examination and this point cannot be stressed too strongly.

MYOSITIS OSSIFICANS

When ossification occurs in the soft tissues, particularly in muscles, it is usually termed "myositis ossificans." There are four types of myositis described (42, 43): (1) progressive, (2) myositis circumscripta, (3) localized myositis (Fig. 24), with ossi-

fication due to injury, and (4) localized ossification (Fig. 25), without a history of injury.

Fig. 25. Ossified hematoma in the lower portion of the left femur. The hematoma followed injury and later ossified.

Various theories have been advanced as to the cause of ossification in the muscles. The most plausible one is that the injury produces a hematoma and the coagulated blood is transformed into bone by way of fibrous tissues and cartilage. A tear of the periosteum may produce new bone formation. Infection in the muscles may be followed by ossification as a repair process.

In the generalized type, muscle bundles undergo transformation into bone without the history of injury. In the circumscripta form, localized ossification occurs from repeated trauma. When this occurs in the adductor longus, it is called "rider's bone" and when in the brachialis, it is known as "fencer's bone."

The *ossification following injury* is the most common type. The bone in the soft tissue is laid down in paths resembling muscle bundles lying parallel to the shaft and never arranged at right-angles. The formation of bone in operative scars is produced by wandering osteoblasts, most likely the result of accidental injury to the ensiform or pubic bones.

In *normal ossification* we deal with an accumulation of lime salts within the stroma or cells of a tissue that has usually undergone certain preparatory changes in the way of formation of more or less homogeneous ground substance but has not suffered a total loss of vitality, though the vitality is possibly decreased.

Pathologic calcification is similar insofar as we have to deal with deposition or partial loss of vitality and which very frequently are hyaline.

Ossification is accomplished only in varieties of connective tissue, but calcification may involve any sort of cell or tissue provided it is degenerated sufficiently. Finally, it should be stressed that any area of calcification is likely to be replaced by bone.

SUMMARY

(1) Various factors contributing to calcification in the soft tissues are discussed.

(2) Illustrations are submitted to show the wide range of possible anatomic sites that may be involved.

(3) There is abundant evidence of calcification occurring in normal and pathological tissues which is frequently of importance from a radiological point of view.

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ROENTGEN THERAPY OF DUPUYTREN'S CONTRACTURE[1]

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DUPUYTREN'S contracture is the term applied to a flexion deformity of the hands caused by thickening and shortening of the palmar fascia. It was first described by the French surgeon, Dupuytren, in 1832. Infrequently this condition is found in the feet.

A definite etiologic factor has not been determined. Trauma, infection, plumbism, and heredity are all factors that have been considered, but as brought out by Meyerding (2) in his series of 273 cases and by many others, none of these is present in a predominant number of cases. The hereditary factor is accepted as being important by most of those who have studied these cases. Trauma is not accepted as being other than a possible predisposing factor. The incidence is relatively low, even an approximate figure being difficult to estimate, but the condition is not rare, as several authors report rather large series of cases.

The pathology is that of a gradually developing contracture of the palmar fascia with increasing flexion deformity of the fingers and palms, usually starting as a nodule at the base of the ring finger and increasing to involve all or part of the palmar fascia and its extensions. The tendon sheaths are not intrinsically involved. The fibrous tissue becomes increased and compact, and lymphocytic infiltration is frequently present.

The condition is usually progressive, tending to involve the entire fascia and produce crippling flexion deformities of the fingers. Occasionally a case becomes stationary. The diagnosis is made on the presence of thickened nodules in the palms at the base of the fingers or from the characteristic flexion deformities of the more advanced cases.

The usual treatment is surgical, and the results, in the hands of a competent surgeon, may be excellent. The technic required is meticulous, requiring skillful dissection and careful preservation of the tendons, nerves, and vessels enmeshed in the tough fibers of the hypertrophied fascia.

The chief objections to surgery are the danger of infection, the possibility of injury to the small but important vessels and nerves, the prolonged period of immobilization in extension required, and the disinclination of many to submit to a rather serious operative procedure.

Little has been written concerning the radiologic treatment of Dupuytren's contracture. In an admittedly incomplete review of the literature but scanty reference to treatment of this condition by the roentgen ray has been found (3). A few papers on radium therapy have been published, but these are confined, as far as can be determined, to the European literature (1, 4).

A method of treatment involving none of the objections to surgical intervention previously mentioned, which can be carried out without loss of time, or the causing of pain or inconvenience to the patient, should, if results are at all comparable, be preferable to surgery. No large series of cases treated by roentgen therapy has been reported, so that statistical comparison is impossible. In any event, the undisturbed anatomy present after roentgen therapy permits the more radical procedure in the event of an unsuccessful result without considerable loss of time, and the fear of surgery frequently inclines the sufferer to years of procrastination while the disease progresses.

The technic of roentgen treatment used in this department is based on the administration of moderate doses of lightly filtered roentgen rays at weekly intervals

[1] From the Department of Radiology and Physical Therapy, University of Wisconsin.

TABLE I

Case	History	Lesion	Treatment	Result
G. W., age 72; white; typesetter: heredity, no	Contracture as result of infection of hands and forearms.	Contraction of fascia to third and fourth fingers of right hand and fifth finger of left.	11–2–34 to 11–13–35; 9 treatments	Right middle finger much improved; right fourth no improvement; left fifth improved.
M. B. R., age 65; white; lawyer	Appearance of swelling and nodule in right palm six months before first treatment.	Firm nodule in palm, right hand.	11–23–31 to 2–22–37; 31 treatments to various fields.	Improvement of primary contractures; pain eliminated; new nodules were resolved as they appeared.
Mrs. J. R., age (?); white; housewife		Nodule in center of right palm 1 cm. diameter, hard and movable.	5–29–34 to 1–29–35; 6 treatments	Marked reduction in size of nodule.
O. S., age 66; white; physician; heredity, no	Nodule appeared 15 years ago. Operated on 1929–1930. Ankylosis left hand.	Contracture of entire palm of left hand and along fourth metatarsal to finger.	6–5–33 and 6–14–33; 2 treatments	No change—no return.
J. R. C., age 78; white; univ. professor; heredity, no	No previous operation.	Marked contracture of third and fourth fingers. Vesicular eruption in palm of right hand.	9–5–30 to 10–7–30; 5 treatments	No change in contracture; eruption cleared; loss of pain. At present slowly increasing contracture.
J. E., age 44; white; heredity, no	Thickening noted for four years in left palm, two months in right.	Marked contracture of left palm over third and fourth tendon sheaths about 3 × 4 cm. Nodule in right palm 1 × 2 cm.	11–4–32 and 11–12–32; 2 treatments	Lost—did not return.
L. B., age 46; white; heredity, no	Cut left wrist in 1906. Operation in 1927 relieved patient for two years. Notes now increased contracture and pain.	Right third and fourth fingers markedly contracted; second less so; left third and fourth fingers contracted less. Unable to close left hand.	8–19–30 to 3–3–31; 8 treatments	Relief of pain without much change in the contracture.
W. H. N., age 52; white; heredity, no	Contractures appeared three years before admission.	Heavy fibrous contractures of right fourth and left fourth and fifth fingers.	5–14–35 to 11–25–35; 11 treatments	Marked improvement in contractures.
N. M., age 48; white; laborer; brother has same condition one hand	Onset since 1928.	Fascia of third and fourth fingers of left hand; third, fourth, and fifth fingers of right hand indurated and contracted.	12–2–36 to 8–25–37; 6 treatments	Fingers of left hand can be extended completely. Result good but less marked in right hand. No pain.
A. R., age 57; white; heredity, no	Slowly progressive contracture since 1921.	Contracture of ring and middle fingers of both hands.	8–26–36 to 9–9–36; 3 treatments	No improvement.

For technic, see text.

for three to four weeks. Several such series may be given at intervals of from six to eight weeks as progress indicates. The technical factors used are: 100 kv., 5 ma., 30 cm. F.S.D., filtration of 1 mm. to 2 mm. Al (H.V.L. in Cu = 0.11 to 0.14 mm.), single doses of from 100 to 200 r (in air), being varied with the thickness and size of the contracture.

We have had the opportunity to observe and treat ten cases of Dupuytren's contracture since 1928, and a summary of our findings is compiled in Table I. Its study shows that in seven out of ten cases treated there was improvement, with loss of pain, reduction of palmar nodes, and relief of contracture. In one or two cases with advanced contracture, the relief of contracture was marked.

It is not our purpose to discourage surgical treatment, but it seems to us that because of the lack of risk of roentgen

therapy in skilled hands, the absence of pain, avoidance of hospitalization and interference with occupation, and the absence of contra-indications one should consider this method of treatment before resorting to the more radical surgical procedure. There are, undoubtedly, some cases which are not good subjects for roentgen therapy and which are more suitable for surgery to begin with. The indications should be carefully worked out for each individual patient with close cooperation of the surgeon and radiologist.

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THE CALCULATION OF PERCENTAGE DEPTH DOSES

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From Columbia University, Institute of Cancer Research, F. C. Wood, M.D., Director

AN analysis of percentage depth dose data reveals some simple numerical relationships which exist between the magnitude of this dose and the size of the portal, the focal distance, and the half value in copper of the incident beam. These relations can be put to practical use in the calculation of approximate doses under widely different conditions of radiation.

The percentage depth dose is found by dividing the intensity measured at a depth by that measured at the surface. The latter consists of the intensity of the beam in air plus that of the back-scattered radiation. These terms are illustrated in Table I by two examples taken from Grebe and Nitzge's tables. In the first example, the surface intensity amounts to 118 per cent (the intensity of the incident beam is called 100 per cent; to this is added back-scattered radiation, which in this case amounts to 18 per cent). The actual intensity at 10 cm. depth is 34 per cent of that of the incident beam. The percentage depth dose is, therefore, $\frac{34}{118}$ or 29 per cent. In the second example, the percentage depth dose is the same as in the first, but the actual depth and surface intensities are not. It is apparent that the percentage depth dose gives no information as to the actual values of these factors from which it is derived. In the following discussion only percentage depth doses at a depth of 10 cm. will be considered.

TABLE I

(*From Grebe and Nitzge*)

H.V.L.	Area	Distance	Surface Int.	Actual Int. at 10 cm.	Percentage Depth Dose
2.00	50 sq. cm.	50 cm.	118%	34%	29%
0.25	400 sq. cm.	40 cm.	136%	39%	29%

I.—THE EFFECT OF PORTAL AREA ON THE 10 CM. PERCENTAGE DEPTH DOSE

The magnitude of the 10 cm. percentage depth dose increases in a definite way with increasing portal areas. The most convenient method of showing this is to compare the magnitudes of doses found under different areas with that obtained under a portal of 50 sq. cm. In Table II are given the results of an analysis of data obtained from various sources. In each case the value of the dose for the 50 sq. cm. area is made unity, and the doses obtained under larger portals are expressed as percentages of the first. Space does not permit the presentation of all of the data;[1] in the table only the averages derived from many ob-

TABLE II.—THE RELATIVE MAGNITUDES OF 10 CM. PERCENTAGE DEPTH DOSES UNDER DIFFERENT PORTAL AREAS, COMPARED WITH THE DOSE UNDER A 50 SQ. CM. PORTAL

	Area of Portal in sq. cm.					
	50	100	150	200	300	400
Holthusen and Braun (3)	100	117	130	138	...	159
Parker and Honeyburne (7)	100	...	132	...	150	...
Mayneord and Roberts (4)	100	115	...	130	...	...
Grebe and Nitzge (2)	100	119	129	137	...	170
Quimby and Copeland (10)	100	117	...	131	...	141
Average	100	118	130	136	150	160

NOTE: The averages here shown are obtained from all of the available data, of which the above are examples.

[1] Complete data referred to in this paper may be consulted at the Crocker Laboratory.

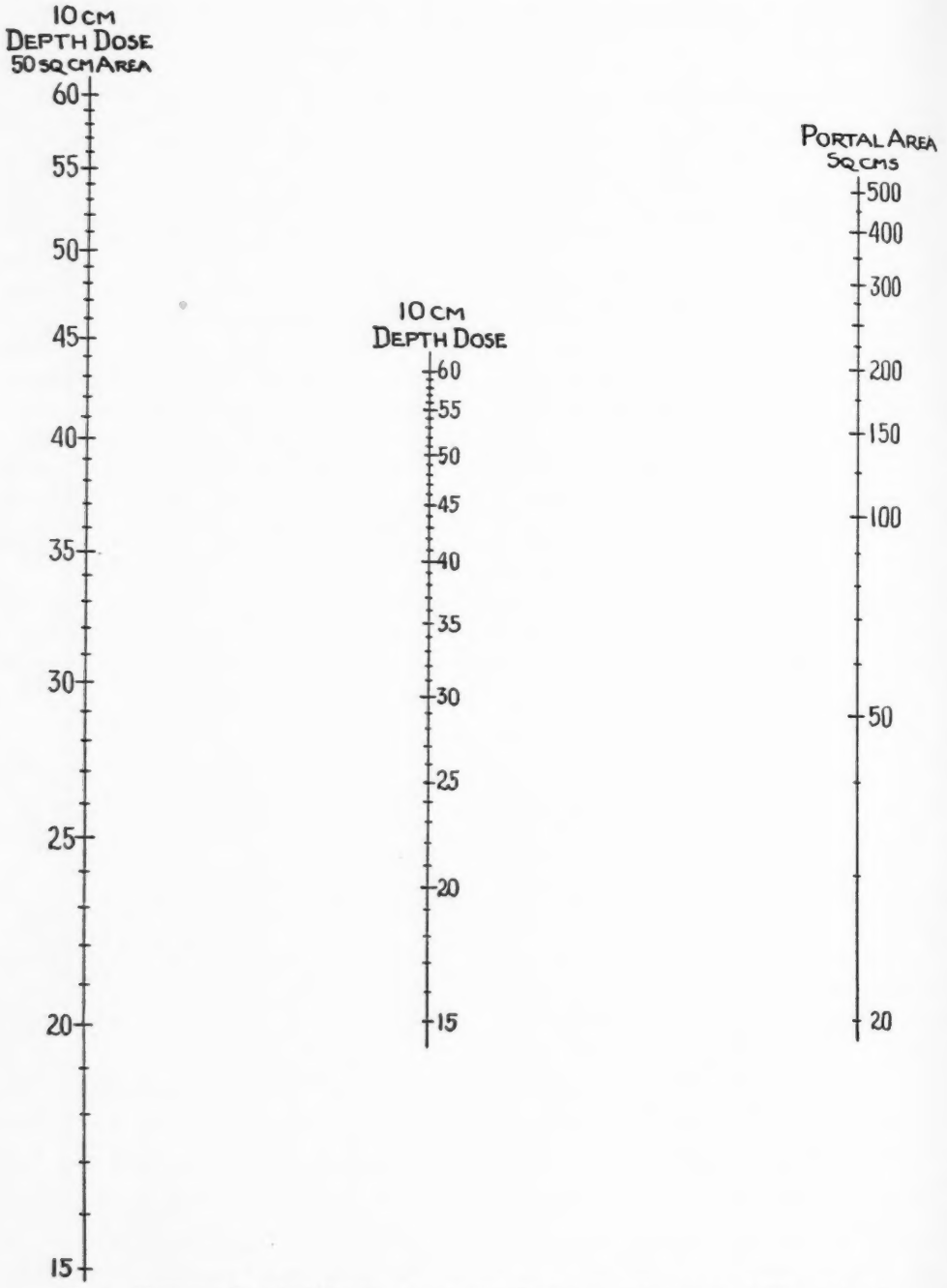

Fig. 1. Nomogram for calculating 10 cm. percentage depth doses under portals of different sizes.*

*Copies of these charts, 8 × 10 in. in size, can be obtained for ten cents each, in stamps, from the Institute of Cancer Research, Columbia University, New York City.

servations are given. In these sets of measurements the focal distances range from 30 to 120 cm., and the half values of the incident beams, from 0.30 to 5.2 mm. of copper. It will be seen that the ratios set down under each portal area agree among themselves fairly well, except those for the largest portal. Here the values given by Grebe and Nitzge are uniformly much larger than any of the others. Those of Quimby and her collaborators are lower than the average. The averaged values of all of the available data are given on the lowest line of Table II. When these are plotted against the logarithms of the areas, they are found to lie along an exponential curve. From this it is possible to determine with reasonable accuracy how much greater or less than the dose under the 50 sq. cm. portal, will be the doses under portals of other sizes.

The nomogram (Fig. 1) simplifies this calculation. With its aid one can readily determine the 10 cm. percentage depth dose under any area, if the dose under a 50 sq. cm. area is known. In making such a calculation it is assumed that the other radiation factors, that is, the focal distance and the quality of beam, remain unchanged. On the left-hand scale are given 10 cm. percentage depth doses under a portal of 50 sq. cm.: on the right-hand scale are shown various portal sizes from 20 to 500 sq. cm. A line passing through the known depth dose value under the 50 sq. cm. portal, and a point on the right-hand scale which marks the area under which the depth dose is to be found, intersects the middle scale at a point which gives the approximate depth dose value for that portal area.

For example, suppose that the percentage depth dose under the 50 sq. cm. portal is known to be 30 per cent; what will be the dose under a 400 sq. cm. portal? The line between the two points mentioned intersects the middle scale at 47 per cent. This, therefore, is the dose under the larger portal. Under a 100 sq. cm. portal the dose will be 36 per cent.

If the depth dose is known for some area other than 50 sq. cm., the doses under larger and smaller areas can readily be found. If, for example, the dose under a 100 sq. cm. portal is known to be 30 per cent, and the dose under a 200 sq. cm. portal is desired (the other radiation conditions remaining the same), the procedure is as follows: a line is passed through the point marked 100 sq. cm. on the right-hand scale and the point marked 30 per cent on the middle scale. This intersects the left-hand scale at 25.2 per cent, which, therefore, is the dose under a 50 sq. cm. portal. Knowing this, the dose under the larger portal may be obtained in the manner first described. It is found to be 35 per cent.

II.—THE EFFECT OF FOCAL DISTANCE ON THE 10 CM. PERCENTAGE DEPTH DOSE

Data showing the effect of focal distance on the 10 cm. percentage depth dose have been treated in the same way as those relating to the effect of different portal areas. The values for this dose, when the distance is 40 cm., are taken as unity, and those for other distances are expressed as

TABLE III.—THE RELATIVE MAGNITUDES OF THE 10 CM. PERCENTAGE DEPTH DOSE UNDER DIFFERENT FOCAL DISTANCES, COMPARED WITH THE DOSE AT 40 CM.

	Focal Distance						
	30	40	50	60	75	80	100
Holthusen and Braun (3)	92	100	107	111	115	...	...
Parker (6)	..	100	...	112	...	116	119
Parker and Honeyburne (7)	..	100	...	108	...	113	115
Grebe and Nitzge (2)	90	100	107	115	...	...	...
Quimby (inverse square law) (8)	88	100	108	114	122	123	129
Average	91	100	107	111	115	115	118

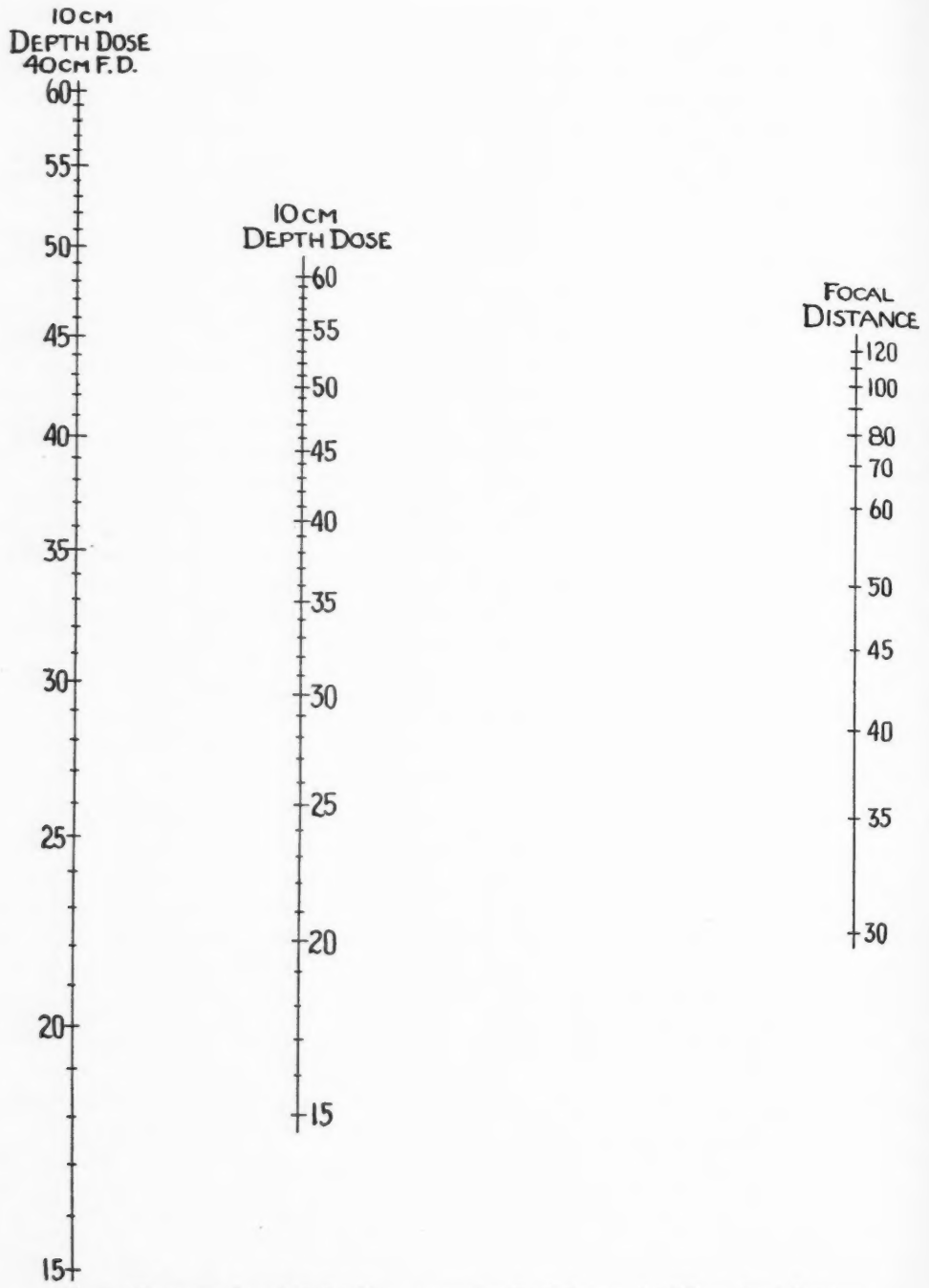

Fig. 2. Nomogram for calculating 10 cm. percentage depth doses under different focal distances.

percentages of these. This particular distance was chosen as a basis for calculation because the majority of investigators have used it in their measurements. In Table

III are given samples of the data. The averages given at the bottom of the table are derived from all of the available data, and, therefore, differ somewhat from those which might be obtained from averaging the figures here presented. It is clear that the ratios are not as consistent as those found in the analysis of results on the effect of area on the depth dose. They differ from the latter also in that they do not fall along an exponential curve. Quimby (8) finds that the increase in the magnitude of the dose with increasing focal distance follows the inverse square law. Grebe and Nitzge's figures conform more or less to this rule, but the extensive data of Parker (6), Parker and Honeyburne (7), and Holthusen and Braun (3) do not, except when the area is small. According to the latter authorities, "the percentage depth dose increases with increasing focal distance more slowly than the inverse square law requires."

Figure 2 is a nomogram based on the data given in Table III. It is used in the same way as the first. The left-hand scale shows percentage depth doses at a focal distance of 40 cm. On the right-hand scale are marked various focal distances from 30 to 120 cm. If the depth dose is known when the distance is 40 cm., doses at greater or smaller distances can be determined by passing a line from the known value on the left-hand scale to a point on the right-hand scale marked for the distance at which the depth dose is to be found. The desired dose is seen on the middle scale at the point where the line intersects it. If the percentage depth dose for some distance other than 40 cm. is known, the doses at any of the distances marked on the right-hand scale can be found by using the method explained in connection with the first nomogram.

III.—THE EFFECT OF THE QUALITY OF RADIATION ON THE 10 CM. PERCENTAGE DEPTH DOSE

The quality of an x-ray beam is usually described in terms of the thickness of a copper sheet which will reduce the radiation to one-half of its original intensity.[2] In the numerous investigations on the effect of different qualities of radiation on the percentage depth dose, the experimental conditions have varied so widely that a direct comparison of results has not always been possible. The portal areas employed have ranged from 20 to 500 sq. cm.; the distances, from 30 to 120 cm. However, all of these data can be reduced, by means of the nomograms, so as to show what the approximate depth doses would be if the area in each case had been 50 sq. cm. and the distance, 40 cm. To illustrate the method of calculation, the following example is offered. In Table IV it is seen

TABLE IV.—TO ILLUSTRATE THE METHOD WHEREBY PERCENTAGE DEPTH DOSES OBTAINED UNDER DIFFERENT QUALITIES OF RADIATION, AREAS, AND DISTANCES MAY BE COMPARED. (*Data from Mayneord and Roberts, 4*)

H.V.L.	Area	Distance	10 cm. % Depth Dose	Depth Dose at 50 cm.[2] and 40 cm. Distance	
2.6	50	75	35	30.8	
2.6	100	75	40	29.4	
2.6	200	75	47	29.6	
2.6	200	122	48	28.9	29.7% ave.
1.2	50	75	32	27.9	
1.2	100	75	38	27.9	
1.2	200	75	43	27.2	
1.2	50	122	34	28.3	
1.2	200	122	44	26.5	27.6% ave.

that when the half value of the beam is 2.6 mm. of copper, the area 200 sq. cm., and the distance 122 cm., the 10 cm. percentage depth dose is 48 per cent. To find the dose when the area is 50 sq. cm.,

[2] The half value layer of the beam may be found in this way. The x-rays, after passing through the filter, are cut down to a narrow beam by a diaphragm. The dosimeter is placed from 15 to 20 cm. below this. The initial intensity is then found. Next, a sheet of 0.25 mm. copper is added to the filter and the intensity again measured. This operation is repeated until the intensity has been reduced to less than half of its original value. The logarithms of the intensities are now plotted against the thickness of copper. Semi-log paper is useful for this. The points which are plotted tend to fall along a straight line. By interpolation, the thickness of copper which reduces the beam to one-half of its initial intensity can be found. This thickness is the half value in copper of the beam.

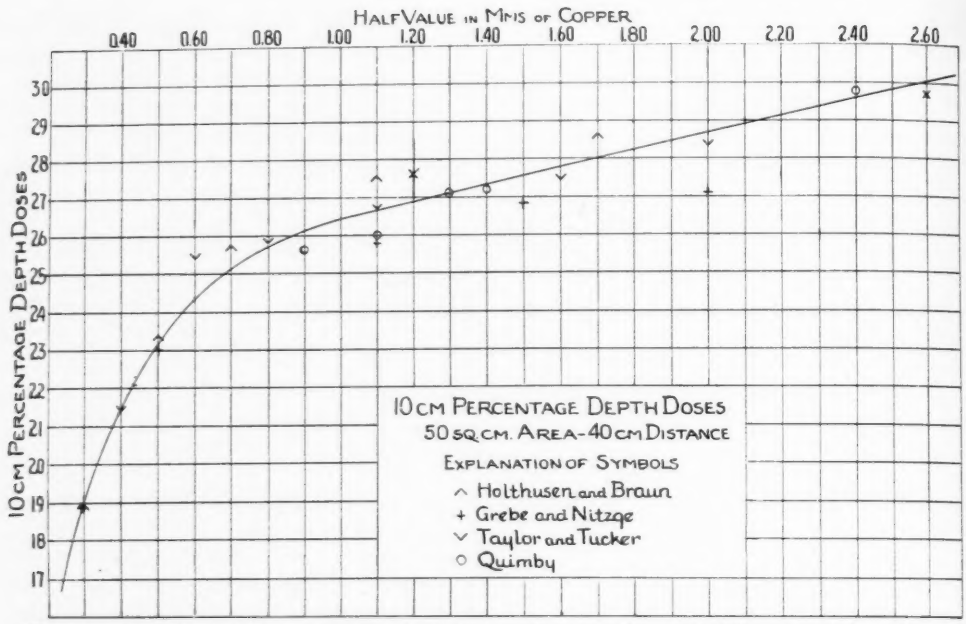

Fig. 3. Chart shows 10 cm. percentage depth doses under x-ray beams of different qualities, when the portal area is 50 sq. cm. and the focal distance 40 cm.

the first or area nomogram is used. A line is passed from the point marked 200 on the right-hand scale, through the point marked 48 on the middle scale. This intersects the left-hand scale at approximately 35 per cent, which is the dose when the area is 50 sq. cm. and the distance 122 cm. To find the dose when the focal distance is 40 cm., the second or distance nomogram is employed. A line passing through the point marked 120 on the right-hand scale and that marked 35 (the value obtained in the first operation), intersects the left-hand scale at approximately 29 per cent. This, therefore, is the percentage depth dose when the half value of the beam is 2.6 mm. of copper, the area 50 sq. cm., and the distance, 40 cm. This value is entered in Table IV in the last column. When all of the data given by Mayneord and Roberts (4) are treated in this way, it is found that those relating to depth doses when the half value in copper is 2.6 are very much alike, the average being 29.7 per cent. Similarly, when the half value of the incident beam is 1.2 mm. of copper, the percentage depth dose, when the area of the portal is reduced to 50 sq. cm. and the distance to 40 cm., is found to be 27.6 per cent.

A large amount of data relating to percentage depth doses under beams of different qualities has been treated in this way. The results shown in Figure 3 were derived from measurements of four groups of investigators, each of whom obtained depth doses under several different qualities of radiation. Other data have been similarly analyzed but are not shown in the figure. The values obtained from Holthusen and Braun's extensive series are, in general, higher than the average; those of Grebe and Nitzge are lower. The differences are not large. The curve drawn to fit the various points must necessarily be a compromise. The maximum deviation from the curve is 1.4 per cent. The curve thus shows with fair precision the 10 cm. percentage depth doses when the portal area is 50 sq. cm. and the distance 40 cm. for all qualities of beams whose half values in copper lie between 0.30 and 2.6 mm. Or, expressed in other terms, for the range of qualities represented by 100 kv. and

0.25 mm. copper filter, and 300 kv. with 3.00 mm. of copper filter.

With this information it is possible to determine, by means of the nomograms, the approximate value of the 10 cm. percentage depth dose within a wide range of areas (25 to 500 sq. cm.) of distances (30 to 120 cm.) and qualities of radiation. The degree to which doses calculated in this way agrees with those obtained by actual measurement is illustrated in Table V. The examples have been chosen to exhibit as wide a range as possible in the experimental conditions of radiation.

TABLE V.—A COMPARISON BETWEEN THE VALUES OF 10 CM. PERCENTAGE DEPTH DOSES OBTAINED BY MEASUREMENT AND BY CALCULATION WITH THE NOMOGRAMS

	H.V.L.	Area	Distance	Percentage Depth Dose	Calculated Depth Dose
Mayneord and Roberts (4)	2.6	200	75	47	47.6
Grebe and Nitzge (2)	2.0	400	50	48	48.5
Parker (6)	1.5	150	100	41	42.3
Holthusen and Braun (3)	0.3	50	40	18	19.0

IV.—THE CALCULATION OF PERCENTAGE DEPTH DOSES AT DEPTHS OTHER THAN 10 CM.

Thus far it has been shown that by means of the figure and the nomograms, 10 cm. percentage depth doses can be calculated with reasonable accuracy for a very wide range of experimental conditions. Next it will be shown that from the values thus obtained it is possible to determine percentage depth doses for any depth below the surface, with the exception of the first two or three centimeters. The reason for this is that when, under various conditions of area, focal distance, and quality of beam, the magnitudes of the 10 cm. percentage depth doses are the same, the doses at lesser and greater depths will also be approximately the same. This relation, pointed out by Holthusen and Braun (3), is illustrated in the data presented in Table VI. In the examples chosen, the 10 cm. dose lies between 38 and 40 per cent; the half values of the beams range from 0.90 to 5.2 mm. of copper; the areas, from 50 to 400 sq. cm., and the focal distances, from 40 to 122 cm. The figures show that the magnitudes of the doses at 8, 6, and 4 cm. depth are much alike, not differing much from the average shown at the right of the table. Other data, not presented here, demonstrate that this relationship is true for other values of the 10 cm. dose. Holthusen (3) remarks that "one may say that for practical purposes, the distribution of dosages in the central beam is determined by the 10 cm. percentage depth dose, independent of the conditions of radiation."

It has long been known that when the logarithms of percentage depth doses are plotted against the depths in centimeters,

TABLE VI.—DATA SHOWING THAT WHEN THE 10 CM. PERCENTAGE DEPTH DOSES ARE EQUAL, THE DOSES AT LESSER DEPTHS ARE APPROXIMATELY EQUAL, INDEPENDENT OF THE CONDITIONS OF RADIATION

Reference		4	4	7	7	4	13	11	2	
Half Value		5.2	2.6	1.5	1.5	1.2	1.0	0.9	0.6	
Area		50	100	50	150	100	400	100	400	
Distance		122	75	60	80	75	50	50	40	ave.
Depth in cm.	10	39	40	40	40	38	38	38	40	39
	8	50	52	50	52	49	50	49	50	50
	6	62	65	62	65	63	64	63	61	63
	4	77	80	77	78	79	80	79	75	78
	2	93	96	91	92	97	94	97	91	94

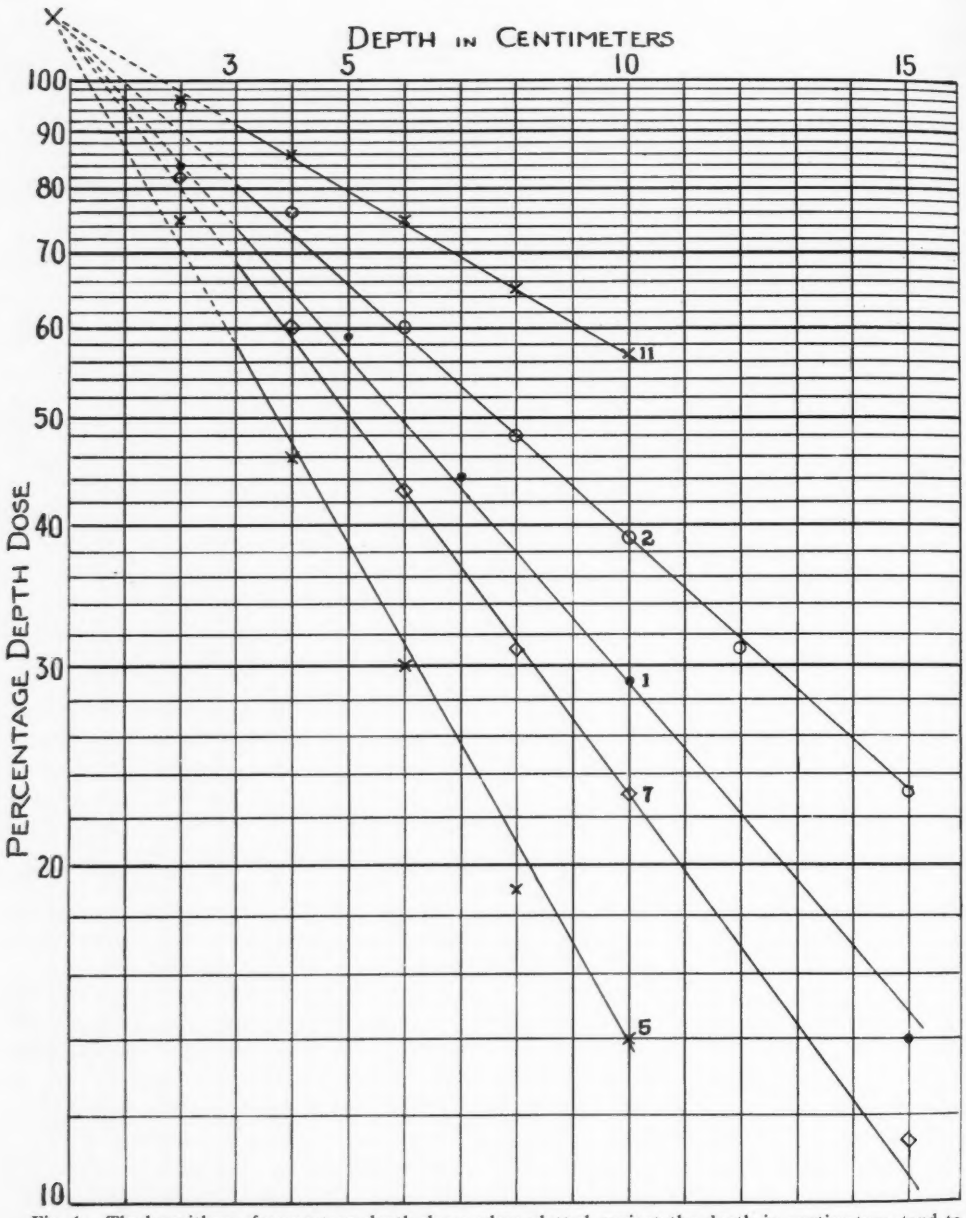

Fig. 4. The logarithms of percentage depth doses when plotted against the depth in centimeters, tend to fall along straight lines. This figure can be used for determining depth doses at various levels, if the 10 cm. percentage depth dose is known For explanation, see text.

the points tend to fall along exponential curves, as shown are Figure 4. The experimental data are taken from various sources to illustrate the wide range of radiation conditions within which this exponential relationship is found. The data for the curve marked 11 were obtained with the use of a beam of 1,000 kv. (11); those for curve 5, from measurements made with a beam having a half value of 0.11

mm. of copper (5). The areas and distances also vary widely.

The straight lines in the figure converge toward a focus which lies somewhat above the 100 per cent point. The reason for this is not apparent. Needless to say, some experimental data plotted in this way fall along straight lines which do not converge precisely on this focus; the divergence, however, is not large. In the figure, the courses of the curves beyond the ordinate for 3 cm. depth are dotted, for actually at about this region the curves change their direction and incline toward the 100 per cent point. But practical use of this exponential relationship which obtains at depths greater than 3 cm. can be made. For if the 10 cm. percentage depth dose is known, either by direct measurement or by calculation with the aid of the nomograms, the doses at other depths, both greater and less than 10 cm., can be found. A line passing through the point indicating the known depth dose and the focus shown in the figure, intersects the ordinates for the various depths at abscissæ which indicate the approximate doses at those levels. The following example illustrates the method, and shows how far the results obtained by calculation agree with those obtained by physical measurement.

The data in Table VII are taken from Parker (6). The conditions of radiation

TABLE VII

(*Data from Parker, 6*)

1.5 H.V.L. 150 sq. cm. Area; 60 cm. Distance					
Depth in cm.	10	8	6	4	2
Measured Values	40	50	62	77	91
Calculated Values	40	49	60	74	90

are given, and the percentage depth doses which were found by actual measurement. Below these appear the doses which have been obtained by calculation in the following way: First, from Figure 3 it is found that with a beam having a half value in copper of 1.5 mm. (the quality used by Parker), the percentage depth dose is 27.5 per cent, the area being 50 sq. cm. and the distance 40 cm. Next, with the use of the first nomogram it is found that under an area of 150 sq. cm. the depth dose is 36 per cent, when the distance is 40 cm. Using this value in the second nomogram, the depth dose, when the distance is 60 cm., is found to be 40 per cent. Finally, on Figure 4 a line is passed through the abscissa for 40 per cent on the ordinate for 10 cm. depth and the focal spot. Along this line the depth doses for depths greater and less than 10 cm. can be found. Some of these are shown in the table. The calculated values do not differ materially from the measured values. In this example, the correspondence is good even at 2 cm. depth. But in general, at depths less than 3 cm. the agreement is not very close. It has already been mentioned that in the region close to the surface, this method of calculating depth doses is not applicable.

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THE IMPORTANCE OF STATEMENT OF TUMOR DOSE IN RADIOTHERAPY[1]

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ONE feels constrained to apologize for the introduction of this somewhat unscientific—I was almost going to say "appeal"—among a series of scientific papers. May I offer as excuse my own difficulties as a beginner in radiotherapy, and my conviction that just as it was necessary to have a universal unit of dosage, so it is becoming important that the many radiotherapeutic clinics in the world should mean one and the same thing when they state dosage.

At the present time there are many different methods in common use of describing dosage. For example, in some clinics the total number of roentgens given to all the skin fields is stated. Other clinics use the even looser form of merely stating the kv., ma., number of fields, and total time of irradiation to a field. Doses are described as measured "in air" in one center, and as "with back-scatter" in another. In radium work, statement of the total milligram-hours is still widely accepted as being a description of dosage, although a slight increase in radium-lesion distance, or of treated area may double them. Statement of dose to tumor is used in still other clinics.

This confusion of expression makes exact appreciation of an author's technic very difficult from reading his articles or hearing his dissertations, and, because of this, hinders the progress of a branch of medicine which is sufficiently tied to the mathematical science of physics to be potentially a fairly exact science itself. It appears particularly unfortunate that no standard method of statement of dosage is in use when it is borne in mind that already an internationally accepted unit of dosage is available for x-ray work, and when there is every reason to believe that doses of x- and gamma-rays can both be measured in terms of roentgens. Furthermore, unlike most other therapeutic agents whose dosage is of necessity described as being the amount given to whole-body exposure *via* the gastro-intestinal tract, hypodermically, or intravenously, irradiation dosage can be stated in terms of the amount delivered to the actual part under treatment.

The patient, after all, presents himself at a clinic for the treatment of his tumor. However the individual radiotherapist may approach the problem of the treatment of his patient, fundamentally he sets out to deliver a dose of irradiation which will be lethal to the tumor, and to deliver it in a manner as little harmful as possible to the surrounding normal tissues. It would appear reasonable, therefore, for him to think and speak and write in terms of the dosage it is necessary for him to give to the *tumor* he is treating, rather than in terms of that given to the normal tissue which he would prefer entirely to avoid irradiating were it possible for him to do so.

Exact knowledge of tumor radiosensitivity is directly dependent upon knowledge of the response of tumors of similar histology to known doses of irradiation. The most obvious way of obtaining information of radiosensitivity is the examination of the results of all the ordinary clinical treatments carried out in as many clinics as possible. This appears to be the only means of reviewing a sufficiently large number of cases to afford reliable data. Statement of tumor dose as the salient item on the routine treatment record sheets is necessary if the material is to be usable for scientific observation of this kind.

Advances in radiotherapeutic technic are the result of experiments carried out because the therapist is dissatisfied with his present work, and believes he can prove

[1] Presented before the Fifth International Congress of Radiology in Chicago, Sept. 13–17, 1937.

more successful by changes in technic. Fundamentally, the best technic he can employ is the one which does maximal permanent damage to the tumor while inflicting least harmful effect to the rest of the patient. A new idea which does not fulfill both these requirements is almost inevitably doomed to failure *ab initio*. Whether or not it is in fact a successful technic and an improvement on its predecessor, can ultimately be ascertained only by using it upon a large number of suitable cases, but it is highly improbable that a technic which, on paper, is a failure will prove a success in clinical use. Precalculation of tissue doses is, then, the first examination of the new idea. For this precalculation to give useful information, it is necessary to know what doses have been delivered to like tumors by the previous unsuccessful technics. This implies the availability of knowledge of tumor dosage throughout the routine work of the clinic.

The teaching of radiotherapy would be greatly simplified if the student were taught to think and work in quantitative terms of radiosensitivity and tumor dosage. At present, he is called upon to learn a large number of technics which, by usage, have been proved successful. These technics, however, are for the most part merely those in use in the clinic in which he works, and do not really give him a very wide view of radiotherapeutic knowledge. When he visits other clinics to broaden his knowledge, he sees methods being employed which are entirely new to him. Unfortunately, he is frequently confused, because not only the technic, but also the terminology used in describing it, is entirely unfamiliar. He is unable to correlate what he is seeing with what he learned in his training school. This fact not infrequently leads the visiting technician to leave a clinic with the erroneous impression that the work there "seems fairly good—but very haphazard," and thus he fails to appreciate the value to himself of what he has seen.

The lesion in an unusual site, to which the standard technics are inapplicable always presents difficulties to the beginner. This is especially so if his approach to the case is, "I think my chief used to give somewhat similar sorts of things about a dozen applications through four or five fields at 200 kv. and 20 ma., and a total skin dose of 3,000 or 4,000 r," and the lesion in question cannot be made to fit into this type of layout. If, on the other hand, he has learned to plan his treatments in terms of "I must deliver x roentgens in y days to that tumor with as little normal tissue damage as possible," his difficulties are greatly reduced. He has to aim at a definite goal defined in physical terms. He can precalculate the value of the various approaches which occur to him, and finally choose the one which fulfills the requirements of the case, or find that he is unable to deliver the requisite dose to this lesion and that, out of fairness to the patient, he must take some course less painful than an attempt at intensive therapy. From the teacher's point of view, it is very much simpler to be able to offer short simple facts about dosage than enter into long descriptions of technic each time he demonstrates a treated case.

In large clinics where several therapists are treating cases of similar type it is almost essential for the standardization of results that the tumor dose be known and recorded. In the Manchester Radium Institute (of whose staff I am a member) it is the custom to precalculate all doses, both radium and x-ray, in roentgens. Graphs show the milligram-hours needed to give 1,000 roentgens for different areas, and different distances, when radium is used, and depth dose phantom charts drawn up for the different tubes and applicators give the necessary information on the x-ray side. The output of the tubes is regularly checked by one of the physicists, but it is not customary to take physical measurements of treatments actually in progress. A complete record of all the factors employed in the treatment is filed with the patient's case notes for future reference. The dose actually given to each

field is entered upon this after every treatment. In a conspicuous position, in a contrasting color of ink, so that it immediately catches the doctor's eye each time the patient attends for follow-up examination, is a statement of:

Method	Radium / X-ray	Tumor dose
	Over-all time	Skin doses.

This is the only information about dosage copied on to the analysis cards of the statistical department.

It is very necessary for rapid advance in radiotherapeutic science that both the routine and experimental work of all centers should be readily comparable. To achieve ready comparability it would appear that, however much detail may be given, simple statement of two things is essential: (1) The result of the irradiation (was the lesion cured, or was it not?); (2) how much irradiation had to be given to achieve that result (what was the tumor dose?).

There are, of course, many technical difficulties in the realization of a universal standard description of dosage, quite apart from those directly related to differing personal opinions. In x-ray therapy the depth dose phantom charts greatly simplify matters. Similar data are available in the use of the radium "bomb." It is, however, essential that the beams from each port of entry shall in fact cross in the tumor for summation of the depth doses to give the tumor dose. Correction for lessened density due to the large amount of air must be made in intrathoracic radiotherapy. When radium is used in the form of multiple sources, either interstitially or on applicators, the physical distribution of the sources must be such as to give homogeneity at the level of the lesion. A reasonable assessment of tumor dose can, however, be stated in any treatment carried out in conformity with modern physical conceptions of radiotherapy, and it is better to make a reasonable or approximate assessment in cases in which the physical difficulties are great than not to attempt ever to state the dose at all.

A plea is, therefore, made for the practice of stating tumor dose as the salient statement in describing radiotherapeutic technic, on the following grounds:

(1) This dose is the basic criterion of any treatment.

(2) It is essential for accurate knowledge of radiosensitivity.

(3) It would simplify the teaching of radiotherapy.

(4) It would greatly aid correlation of the results obtained in various clinics.

THE FOCALOGRAPH

A NEW METHOD FOR EXAMINING THE TARGET OF A ROENTGEN-RAY TUBE[1,2]

By CAPTAIN EDWARD K. REID, A.B., M.D., Medical Corps Reserve, *and* STAFF SERGEANT LAWRENCE F. BLACK, Medical Department, U. S. Army

From the Department of Roentgenology, Army Medical School, Lieut. Colonel W. W. McCaw, Medical Corps, Director, Washington, D. C.

MANY methods have been proposed for the examination of the target of an x-ray tube. It must be conceded that any method which provides a permanent record for comparison has advantages over methods which do not have this feature.

The device described, the Focalograph, as proposed by Sergeant Black is a simple, economical, and efficient apparatus for:

(*a*) Providing a record of the appearance of the target of a roentgen tube. (By enlargement obtained by increasing the grid-film distance it is possible to see minute defects plainly.)

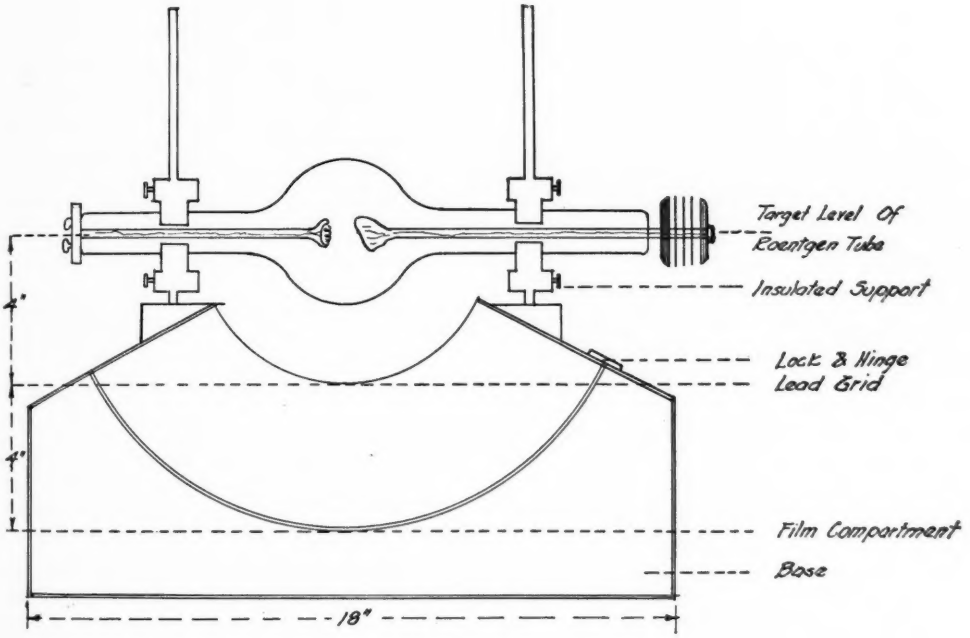


Fig. 1-*A*.

(*b*) Demonstrating the effect of angular position of the target of a roentgen tube upon the effective ray.

(*c*) Checking the effective area, actual area and minimum projected area of the focal spot of a roentgen tube. This is especially valuable in checking performance of tubes against specification claims.

(*d*) Determining the maximum ray divergence and minimum focal film dis-

[1] Approved by the office of the Surgeon General, U. S. Army, Washington, D. C.

[2] This paper approved for publication purposes only. The authors' opinions are their own and for which the Surgeon General's Office accepts no responsibility.

tance for various types of tubes as they are affected by the angle of the target face.

The apparatus described consists of a simple wood-constructed tube holder for the roentgen tube with a special accurately

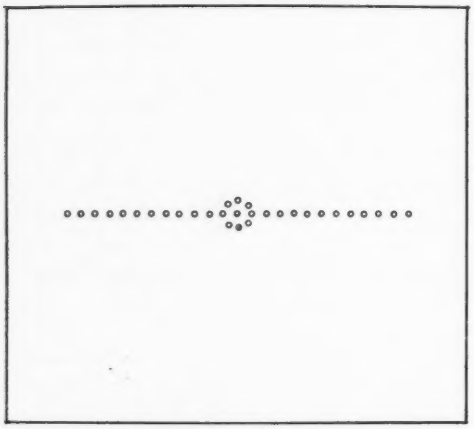


Fig. 1-*B*.

perforated lead diaphragm placed on an arc between the tube and a film which is to be exposed for record (Fig. 1-*A*).

It is also possible to study the lateral divergence by use of grids constructed in that plane. It is conceivable that many methods of grid construction may be applied to the basic apparatus in the future. The grid shown is the best found as yet for comparison studies, as it is possible to obtain several exposures on the same film.

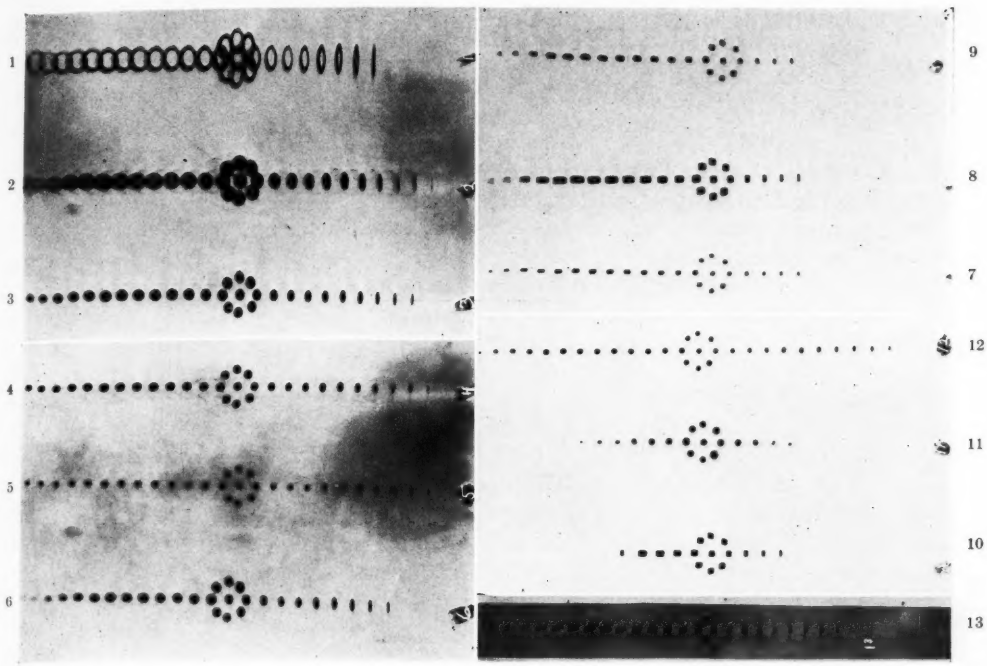
The tube is enervated from a regular x-ray machine in the usual manner.

The arc of the film and of the lead diaphragm is so constructed that the appearance of the film exposed is the same as the composite image obtained by many horizontally placed films exposed with the target placed at various angles. The saving in film for experimental purposes in this procedure is obvious.

It is recommended that the following technic be used in making the records described: kv.p., 40; ma., 10; sec. 10. The distance of the target to the lead grid is not to exceed 4 inches; the usual film distance is set by the apparatus. Cardboard film holders are used. Enlargements may be made by increasing the distance to the film. Under no circumstances may the kilovolt peak be increased above 40, as the danger of spark-over through the lead grid is imminent.

DESCRIPTIVE DATA

1. Westinghouse Treatment Tube, tungsten disc (Fig. 1):
   Dark ring— Actual focal spot.
   Lighter halo— Margin of focal spot.
   Wide halo— Outside edge of entire anode.
2. Universal Broad Focus, solid tungsten anode (Fig. 2):
   Dark center— A crater on surface.
   Light ring— Flat surface.
   Dappled outer dark ring— Melted raised areas on target.
   Outer halo— Outer margin of anode.
3. Universal Medium Focus, solid tungsten anode: good condition (Fig. 3):
   Dark— Actual focal spot.
   Halo— Anode.
4. Universal Fine Focus, solid tungsten anode: good condition (Fig. 4):
   Dark— Actual focal spot.
   Halo— Anode.
5. So-called Self-rectified Tube, 5–10, solid copper anode containing a tungsten button: good condition (Fig. 5):
   Dark spot— Tungsten focal spot.
   Halo— Copper anode.
6. Gas Tube (over 30 years old) (Fig. 6):
   Appears to be platinum face and copper back. The density of this spot is not the same as of the other tubes due to the drop in kv.p. caused by the amount of resistance in the circuit.
7. X-P 1. Small side (Fig. 7):
   X-P 1–4. General Electric Double Focus Tube (Line Focus):



Figs. 1–13.

New Benson Focus Tubes, copper anode with tungsten button embedded.
Dark spot— Actual focal spot.
Medium halo—Outer ring of tungsten.
Outer halo— Copper anode.

8. Large side of Double Focus, X-P 1–4, General Electric:
Also 20° anode (Fig. 8):
Dark spot— Actual focal spot.
Medium halo—Outer ring of tungsten.
Outer halo— Copper anode.

9. Westinghouse Line Focus Fluoroscopic Tube, copper anode with tungsten button (Fig. 9):
Dark spot— Actual focal spot.
Medium halo—Outer ring of tungsten.
Outer halo— Copper anode.

10. Philips Metalix 6 K.W. Tube, copper anode with tungsten button (Fig. 10):
Dark spot— Actual focal spot.
Medium halo—Outer ring of target.
Outer halo— Copper anode.
The small dark spots in the halo outside of focal spot are pins of tungsten holding the tungsten button in place.

11. Westinghouse Right-angle Dental Tube, copper with tungsten button (Fig. 11):
The filament is a tantalum ring through which both the cathode ray and x-ray pass in opposite directions. The effective size is the actual size. The halo is probably the filtration effect of the tantalum filament.
Dark spot— Focal spot.

12. Right-angle Dental General Electric, copper with tungsten button (Fig. 12):
Note the very small amount of halo.
This is old type tube and cathode, anode internal distance is very great.

13. Is a defective tube split target which was replaced by manufacturer upon the strength of this picture (Fig. 13).

CONCLUSIONS

1. A device is presented for experimental investigation of roentgen-ray tube targets.

2. It is hoped that the low cost of this device will permit its adoption in many clinics, and as a consequence of its use many previously unknown facts may be brought to light.

3. Some of the results obtained with this device are demonstrated.

BACK-SCATTER AND ITS EFFECT ON DOSAGE MEASUREMENTS[1]

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THE rationale for the use of voltages in excess of 200 kv.p. in x-ray therapy is, first, the greater depth dose obtainable, and second, a more favorable biologic reaction. The latter is problematical and is one which the clinical radiologist will have to prove or disprove as he gains more experience. The first is a perfectly definite physical problem, susceptible of relatively accurate physical measurement. It is the purpose of this paper to discuss one important aspect of this measurement, and thus enable the radiologist to avoid what might otherwise be a serious error in his concept of dosage.

Percentage depth dose is the ratio of the amount of radiation being absorbed at a given depth to the amount of radiation being absorbed by the skin. This percentage may be increased by increasing voltage to the x-ray tube, by increasing filter thickness, by increasing target-skin distance, and by increasing area or volume of tissue being radiated. As the area or volume of tissue increases the depth dose increases, due to an increase in scattered radiation. It is on this factor that we will concentrate our attention.

When an x-ray beam strikes a body such as human tissue several different things happen. Part of the radiation passes through the body unabsorbed and unchanged. Part of the radiation is absorbed. The energy of this absorbed radiation is used in ejecting an electron from the absorbing atom. It is the action of this secondary electron which is probably accountable for all the chemical, physical, and biologic effects of x-rays. Still another part of the primary radiation is scattered when it strikes the body. That is, it is bent out of the straight line which it was traversing from the anode of the x-ray tube to the point of scattering. This scattering is analogous to the effect on a beam of visible light when a ground glass is interposed into its path. The light rays are bent from their original path, and the resultant image of the light source on the retina of the eye is blurred and hazy. There is no change in wave length of the visible light when it is scattered. Thus a red light, when viewed through a ground glass is still red. When x-rays are scattered, the result is different. There is a slight change in wave length, and most of the scattered rays are slightly longer than the primary unscattered rays. This change in wave length is so small that it was not until 1922 that its effect was noticed. Previous to that time it was thought that the scattered radiation had the same wave length as the original unscattered primary rays. Professor Compton, of the University of Chicago, made the experimental discovery of this change in wave length. The work was of such fundamental importance that he was awarded the Nobel Prize in Physics. For practical purposes, however, we can consider scattered radiation as having the same penetration as unscattered primary.

Scattering takes place in all directions in respect to the primary beam, with the greatest amount in the forward direction. However, some is scattered directly backward, and this portion of the scattered radiation is called back-scatter. Scattered radiation obviously plays an important rôle in dosage because it increases the amount of radiation being received by any given volume at any point in or on the radiated body. Obviously, the greater the volume being radiated, the greater the number of scattering sources, and hence the greater will be the radiation intensity at any given point within this volume.

[1] Presented before the Fifth International Congress of Radiology, at Chicago, Sept. 13–17, 1937.

This accounts for the increase in depth dose with increasing size field. It similarly plays an important rôle in skin dosage because the back-scatter increases the amount of radiation being received by the skin by just that amount which is being scattered back to the skin from the underlying tissues.

Most measurements, as made in the United States, are made in free air. This means that the ionization chamber which absorbs the radiation being measured is placed sufficiently far distant from any solid body so that no back-scatter reaches it. Obviously, if we so measure, we do not have a true indication of the amount of radiation which the skin is receiving. The skin is receiving, in addition to what we measure, the amount due to back-scatter. This amount is dependent upon the quality of the radiation and upon the size of field being radiated. In view of this, why do we not at all times measure with back-scatter, that is, with the ionization chamber on the surface of the body, instead of in air? In the first place, from a strictly scientific point of view, the definition of the International Roentgen definitely excludes scattered radiation. Secondly, there are certain inherent technical difficulties in measuring with back-scatter which render determinations, as made by the average radiologist in his own x-ray department, subject to rather serious experimental errors. For example, the precise position of the ionization chamber in respect to the skin surface plays an important part in the readings. A chamber placed on the skin will register considerably different from one half-buried in the skin (as it should be). It has been the author's practice to make all measurements in free air, and then to calculate from these the tissue dose on the skin which includes the sum of the incident and the back-scattered radiation. Back-scatter determinations were made once, under carefully controlled conditions, and from these data the calculations are made. In this way, the errors of measurements made under practical laboratory conditions are eliminated. All measurements were made with a thimble type ionization chamber. While these measurements are subject to the errors described by Quimby before a previous International Congress, they are made on the same basis as most other measurements in this country and so can at least be used for comparative evaluations. The back-scatter data which the author uses are shown in the following table:

TABLE I

Field Size	Percentage Back-scatter			
Wave length:	0.15	0.25	0.40	0.80
25 sq. cm.	16	13	6	2.5
100 sq. cm.	30	23	13	7.0
200 sq. cm.	38	27	16	8.0
300 sq. cm.	43	30	18	8.5
400 sq. cm.	45	32	20	9.0

This table shows an interesting sidelight on the effect of back-scatter from a practical clinical side. In deep therapy the field size is usually large, seldom less than 15 × 15 cm. From the table it may be seen that there is relatively little change in back-scatter with different large size fields. On the other hand, in skin or superficial therapy in cases in which there are large differences in field size used, the total amount of back-scatter is small with any size field. Thus, once a proper technic is established, it is almost unnecessary to make allowances for different size fields, as any errors are almost automatically eliminated by the manner in which x-ray therapy is administered.

However, in estimating depth dose, the relation of scatter to air measurements must be fully understood in order for one not to be misled in regard to the tissue dosage being given. All depth dose measurements must be made inherently with back-scatter. The ionization chamber is first half embedded into the surface of the phantom for surface readings, and then totally into the phantom for depth readings at the required depth. Under these conditions the measurements necessarily include back-scatter. Ordinary clinical dosage measurements are made in air, and it has been my experience that many

radiologists think of dosage at the depth measured with scatter in terms of their ordinarily used air measurements. If the dose as measured in air is 200 r and the percentage depth dose is 40, the actual tissue dose to the depth is not 40 per cent of 200, as is so commonly assumed, but is 40 per cent of the skin dose, which would be 40 per cent of 200 plus the back-scatter. Assume that the back-scatter is 45 per cent; 45 per cent of 200 is 90, which makes the skin dose 290 r; 40 per cent of this skin dose would be 40 per cent of 290, or 116 r. If we had not included back-scatter, we would have calculated 40 per cent of 200, or 80, as the tissue dose. If we wish to think of percentage depth dose in terms of air measurements, which I think might be perfectly permissible, we must use as a percentage depth dose the ratio of 116 r to 200 r, or 58 per cent. If we consider the relation of skin dose to depth dose, the percentage is 40. If we consider air dose to depth dose, the percentage is 58.

This is of especial importance when considering depth doses at voltages higher than 200 kv.p. With the more penetrating radiation delivered at these higher voltages, the percentage of back-scatter decreases. Table II shows this quantitatively:

TABLE II

KV.P	Percentage Back-scatter
200	43
250	37
300	31
350	26
400	24

With 20 × 20 cm. field and 3 mm. copper filter.

Table III shows the increase in percentage depth dose with increasing kilovoltage:

TABLE III

KV.P	Percentage Depth Dose
200	42.5
250	45.0
300	45.5
350	45.8
400	46.0

With 20 × 20 cm. field, 3 mm. copper filter, 60 cm. distance.

Let us now compare depth doses at 200 and at 400 kv.p., and see how extremely important it is to understand fully the implications of scattered and air measurements.

For every 200 r measured in air at 200 kv.p., there would be 42.5 per cent of (200 plus 43 per cent back-scatter); 43 per cent of 200 is 86, giving a skin dose of 286 r. Taking 42.5 per cent of 286 gives us 123 "tissue roentgens."

For every 200 r measured in air at 400 kv.p., there would be 46 per cent of (200 plus 24 per cent back-scatter); 24 per cent of 200 is 48, giving a skin dose of 248. Taking 46 per cent of 248 gives us 114 "tissue roentgens."

This is rather startling, for it tells us that if we make our measurements in air, the same dose will give less tissue dose at 400 kv.p. than it will at 200 kv.p.

If, however, we measure with back-scatter, the effect will be the expected one. In order to get a true picture, we must compare depth doses with equal skin doses—not with equal air doses. With equal air doses, the skin dose is less with 400 kv.p. than it is with 200 kv.p. and the depth dose is also less. To get comparable depth doses, we must administer 287 r at the skin with 400 kv.p., which will give us a proper equal basis for comparison. The tissue dose with 400 kv.p. then becomes 45 per cent of 286, or 132 r, as compared with 123 r at 200 kv.p.

The skin dose with 200 kv.p. is 286, while the skin dose with 400 kv.p. is 248, the former being 15 per cent more than 248; it therefore takes 15 per cent more r as measured in air to give the same tissue depth dose with 400 kv.p. as with 200. The practical result of this is that the radiologist who has been accustomed to administering 200 r in air at 200 kv.p., and who then changes to 200 r in air at 400 kv.p., is actually giving less radiation to the depth at 400 kv.p. than he was at 200. Hence, in order that proper advantage may be taken of the slight increase in depth dose of 400 kv.p. over

200 kv.p., it is essential that all measurements be made on the basis of surface readings, or at least, if made in air, be properly correlated to surface readings. Certainly, the radiologist must become more constantly cognizant of the interrelationship between the dose as measured and administered under air beam control, and the dose as delivered to skin and to tissues within the body.

SOME FACTORS INFLUENCING THE DISTRIBUTION OF RADIATION USING A TWO-OBLIQUE-FIELD TECHNIC

By M. C. REINHARD *and* F. MIERS, *Buffalo, N. Y.*

From the State Institute for the Study of Malignant Diseases:
Burton T. Simpson, M.D., Director

IN the treatment of pelvic malignancies by means of x-radiation, there has been during the past decade a progressive increase in the target-skin distance, resulting in an increased intensity at depth. To-day 200 kv. x-ray treatments are given at target-skin distances of 80 centimeters or higher. Obviously the simplest technic is to use one large 20 × 20 cm. field anteriorly and posteriorly. The large field radiates the entire pelvis and due to the scattering from such a large volume of irradiated tissue, the depth intensity at a point 10 cm. below the skin may be as high as 50 per cent of the skin dose. Mattick (1) has published tables simplifying the procedures in calculating the dose by this technic.

In cases in which still greater intensities at depth are desired four or even six fields may be applied. Following the suggestion of Weatherwax (2) long narrow rectangular fields should be used, two anteriorly and two posteriorly (and two lateral) and the radiation directed so as to overlap in the midpelvic region. This latter method was adopted at the State Institute several years ago with the angulation of the beams and the separation between the two anterior and two posterior ports predetermined. In view of the fact that the patient was treated at one sitting with only one, or at most two, ports per day over a period of from 40 to 50 days, a variation from day to day in the angulation or spacing of the ports could be very easily introduced. The question arose, therefore, as to how significant such slight daily variations might be in routine treatments.

The present paper deals with ionization measurements made in a water phantom which was radiated by two simultaneous beams of radiation in order to arrive at some conclusions regarding variations in the set-up and the resulting errors.

The physical set-up for these measurements was as follows:

Two XPT type tubes excited simultaneously by one generator, were operated at 200 kv.p. and 10 ma. The intensity in air and the half-value layer of copper were determined for each tube separately with the radiation from one of the tubes cut off by means of a lead shutter. The output from each agreed with that of the other and, in addition, the quality of the beam was the same as with a single tube operated at the same voltage and 25 ma., namely, 1.0 mm. copper half value layer.

Each tube could be rotated on its long axis so as to permit the adjustment of the angulation of the two beams. The radiation from both tubes was confined and directed by means of wood treatment cones lined with lead rubber for the entire treatment distance of 80 centimeters. The fields were 10 × 15 centimeters. With the long axes of the fields parallel the radiation was directed into the water phantom with the following angulation and spacing:

1. Each beam inclined 6° away from the perpendicular.
2. Each beam inclined 11° away from the perpendicular.
3. Each beam inclined 16° away from the perpendicular.

A second adjustment was provided so that the phantom end of the treatment cones in each of the three angulations could be touching, separated 2 centimeters or 4 centimeters, giving, in all, nine combinations.

The water phantom was 32 × 50 × 26 cm. high, with provision made to insert a thimble ionization chamber at various

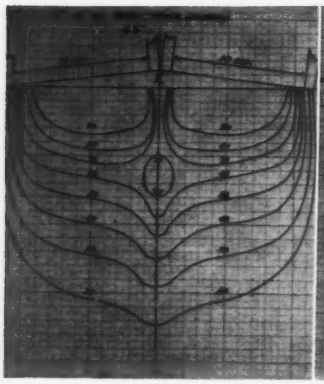

Fig. 1.

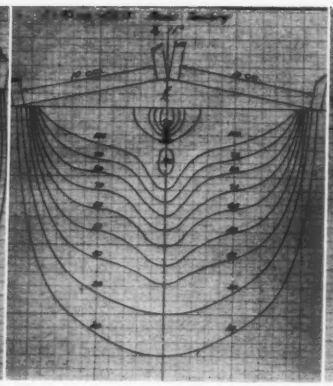

Fig. 2.

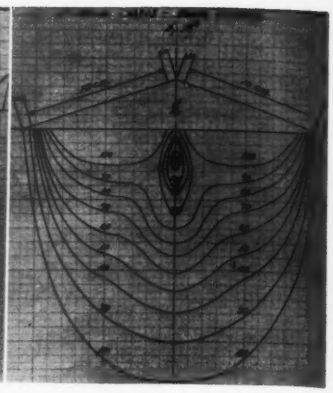

Fig. 3.

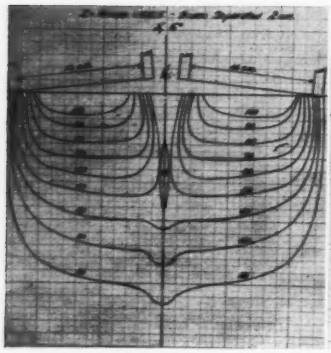

Fig. 4.

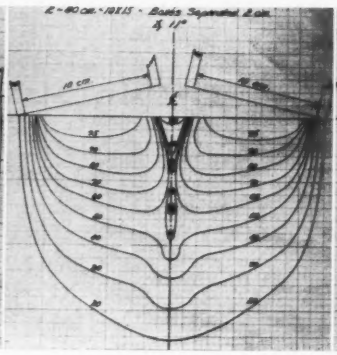

Fig. 5.

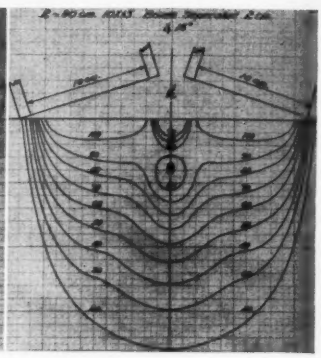

Fig. 6.

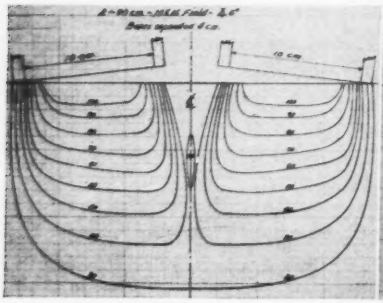

Fig. 7.

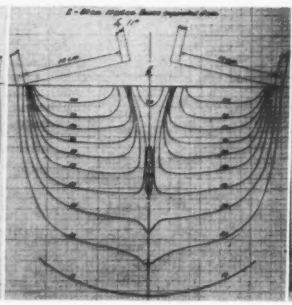

Fig. 8.

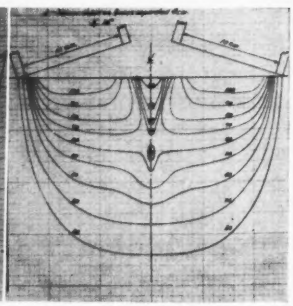

Fig. 9.

levels. The phantom was supported on a track, so that it could be moved horizontally in two directions by means of racks and pinions. A thimble type ionization chamber was used in conjunction with a Victoreen condenser r meter. The intensity was measured at centimeter intervals below the surface, along the center line and at lateral distances of 1, 2, 3, etc., centimeters to the right (or left) of the center line. The values so obtained were related to the 100 per cent intensity on the

surface immediately below the center of either treatment cone, and curves were constructed for the depth intensities at the various positions. Figure 10 shows part of a family of such curves.

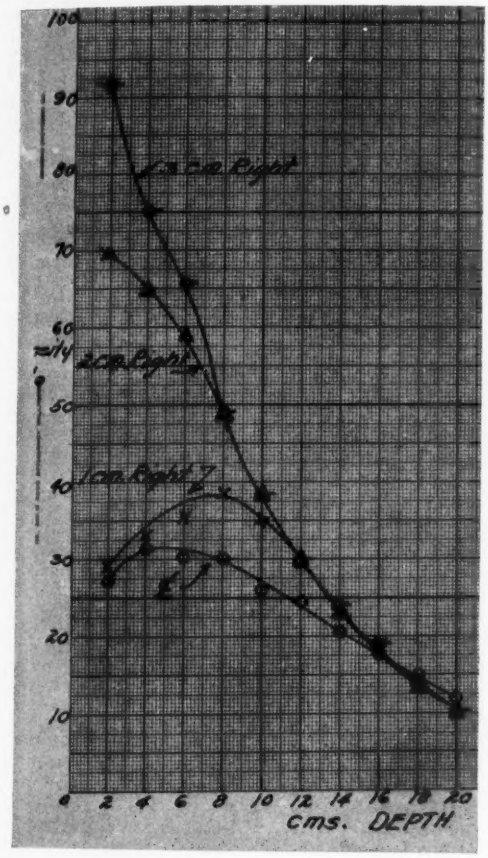

Fig. 10. Two 80 cm. 10 × 15 boxes separated 4 centimeters.

From such families of curves, one lateral half of the final isodose curve was constructed, the other half being, of course, merely a mirror image of the first half. The nine complete isodose curves are shown in Figures 1 to 9, representing the three angles, 6°, 11°, and 16°, and the three separations, namely, touching, 2 centimeters and 4 centimeters between the two cones.

OBSERVATIONS

First.—The distribution of the radiation and the relative intensities at the different depths are somewhat different than that which would be obtained by superimposing two separate isodose curves. The difference may be due to the fact that the ionization chamber measures the average intensity for a definite volume, whereas in the latter condition the intensity is obtained by a summation of the intensities from the two separate curves at a point below the skin.

Second.—These curves indicate the angulation and spacing necessary to avoid or to produce so-called "hot spots" where desired, as the particular case to be treated may require.

Third.—A daily variation in the setting up of a patient on whom only one area is treated at a time, could very easily result in a marked difference in the amount and distribution of the radiation in the region in question.

Fourth.—Isodose curves obtained from measurements made when only one beam of radiation was used, agree with those published by May (3) for the same angulation.

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APPLICATION OF ROENTGEN RAY IN DIAGNOSIS OF CONDITIONS OF THE THYMUS GLAND IN CHILDREN[1]

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FOR practical purposes, the conditions of the thymus gland in children which require consideration are: (1) Enlargement or hyperplasia. It has been felt for many years that the thymus, resting in close apposition to the trachea and great vessels and nerves at the point where they come through the rigid bony superior thoracic inlet, may, by its enlargement, so compress these important structures as to produce obstructive symptoms such as dyspnea, stridor, coughing or choking, and cyanosis, at times to the point where asphyxiation and death may result. (2) The condition of status thymico-lymphaticus, described as a combination of constitutional hereditary anomalies which includes preservation or hyperplasia of the thymus, hyperplasia of the lymphoid tissue of the intestines, spleen and elsewhere, with hypoplasia of the aorta and cardiovascular system and of the adrenals. Such individuals may suddenly die from the most trivial causes, and it has been thought that the finding of a large thymus may be a direct indication that this diathesis exists. Others believe that this condition may exist without obvious enlargement of the thymus.

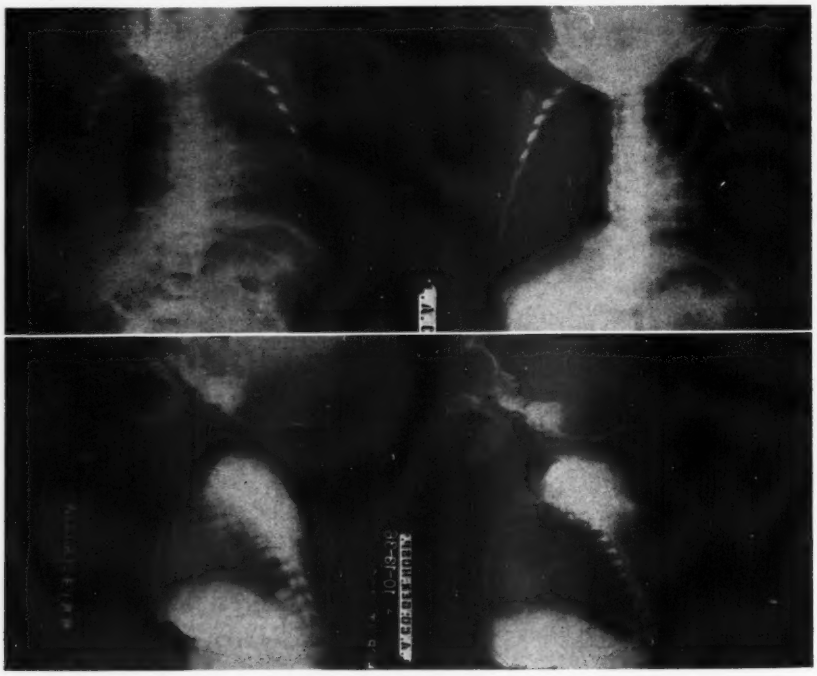

Fig. 1. Normal appearance of the chest (see text). Upper views taken in the supine position, at the left in expiration, at the right in inspiration. Lower views taken in the lateral position, at the left in expiration, at the right in inspiration.

[1] Much of the material presented is used through the courtesy of Dr. Oscar Reiss, Chairman of the Department of Pediatrics, Los Angeles County Hospital.

ROENTGEN DIAGNOSIS

The application of the roentgen ray may be of diagnostic aid in these conditions in the following ways: (1) in showing enlargement of the gland; in detecting pressure phenomena, particularly of the trachea; the possible diagnostic value of a therapeutic test with roentgen rays.

Normal Roentgen Appearance.—The normal infant's chest, so well described by Wasson (1) in his observations on the anatomy of the thymus gland, shows in the anteroposterior views (Fig. 1) two auricles and the great vessels forming the base of the heart shadow, the superior vena cava at the right and the pulmonary artery on the left. The aorta lies in the midline; only in later life does it project to form the aortic arch. These structures form a triangular shadow which narrows as it passes upward toward the first rib. At its narrowest point it is less than the diameter of the spinal column. The trachea is in the midline behind the aorta, bifurcating at about the third thoracic vertebra; the esophagus lies behind the trachea and is not seen. The thymus is included in the superior mediastinal shadow, its base overlapping the base of the heart. It is usually widest at the third interspace. In the recumbent postero-anterior position at full inspiration, the normal mediastinal shadow at the second interspace is about one and one-half times the width of the body of a dorsal vertebra. The lateral view should show the pharynx, posterior border of the tongue, epiglottis, vestibule of the larynx, retropharyngeal space, and

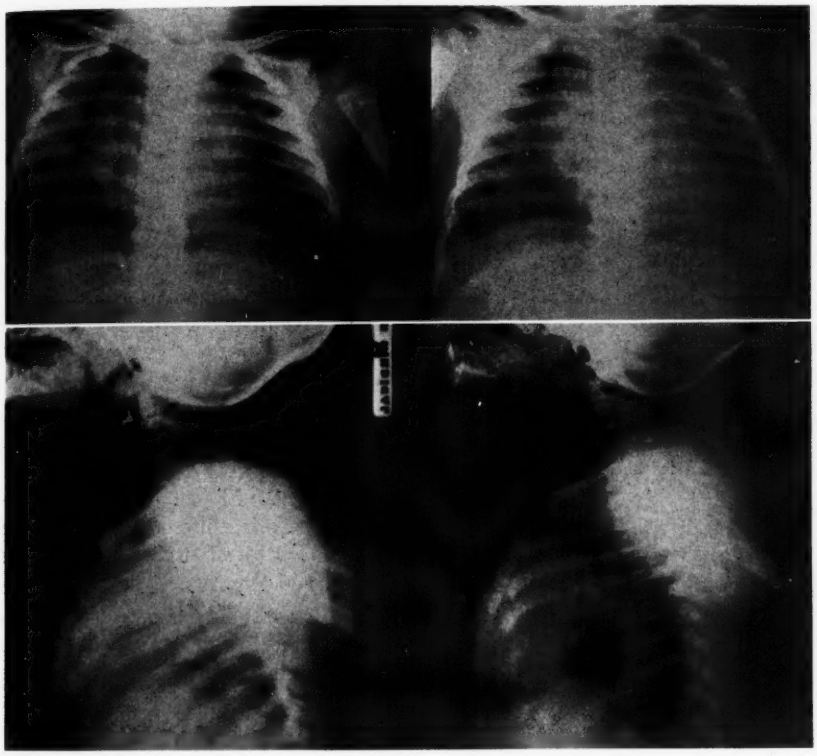

Fig. 2. Definitely enlarged thymus. Thymic shadow nearly 8 cm. wide and over four times the width of the thoracic vertebra. Narrowing of the trachea in the lateral view.

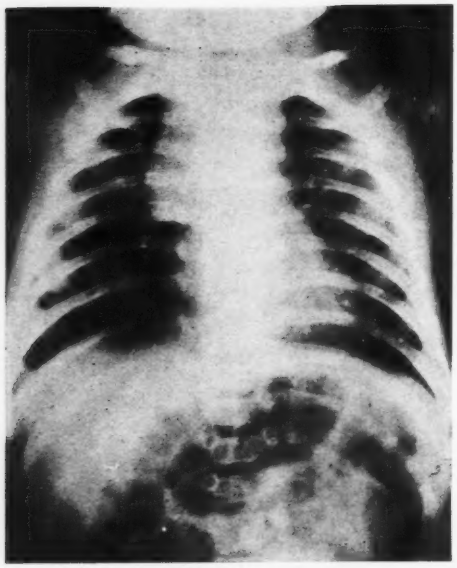

Fig. 3. Large thymus, slightly squared keystone-shape, 4.5 cm. wide, three times the width of the thoracic vertebra. Right lobe a little larger than the left: trachea in the midline. (*This film used through the courtesy of M. L. Pindell, M.D., Los Angeles.*)

the trachea. There may be slight buckling or narrowing of the trachea, but no definite constriction or collapse.

Thymic Enlargement.—Upon what basis should the thymus be called "enlarged," or said to be producing pressure? Wasson (1) says twice the diameter of the vertebra at the second or third interspace is a thymus of moderate size; three or more times the diameter is a large thymus.

Friedman (2) considers the normal upper mediastinal shadow as 3.5 cm. in width in children under three. However, there is such wide variation that it is difficult to give definite measurements. Thus Kinney and Taylor (3), in a study of 160 consecutive infants, roentgenographed within 24 hours of birth, found no normal thymus shadow as to size, shape, or density: 54 were less than 3 cm. in width at the level of the third dorsal vertebra; 36 were 3 cm., and 70 over 3 cm.

Pancoast (4) stresses the importance of a lateral view, placing particular significance upon collapse or buckling of the trachea at the thoracic inlet in deep inspiration.

Both Pancoast and Hasley (5) emphasize the value of thorough fluoroscopic examination in all positions before a positive diagnosis of enlargement can be made. Figures 2 and 3 are examples of a definitely enlarged thymus.

Differential Diagnosis.—Accurate uniform radiographic technic is essential to avoid mistaken diagnoses. Thus, incorrect position may so distort the shadows as to give a spurious appearance of enlargement of the thymus or of buckling of the trachea. This is illustrated in Figure 4, in which partial rotation of the patient in the lateral view has distorted the outline of the trachea.

The mediastinal structures in infancy and childhood are not fixed but move freely, changing size, shape, and position constantly during the respiratory and cardiac cycles. Figure 5 shows to what extent the respiratory phase may modify the picture and lead to a faulty impression of enlarged thymus.

In films which are correctly taken during inspiration, the widening of the superior mediastinal shadow is nearly always due to the thymus, especially in the very young. Tumors, causing enlargement, are very rare and are usually found in older children. An intrathoracic thyroid causes a mediastinal widening, but this is usually broad above and narrow below. It may be unilateral and it is almost always seen in adolescents and adults. Tuberculous adenitis also occurs in children, but gives a shadow usually denser and wider at the roots of the lungs. Figure 6 is an example of this disease.

Far more important and difficult than the conclusion as to whether or not a thymus is enlarged is the clinical application of the roentgen findings of a large thymus. In any given case in which a large thymus has been demonstrated, is this large thymus the cause of all or part of the child's symptoms or, if a large thymus is found

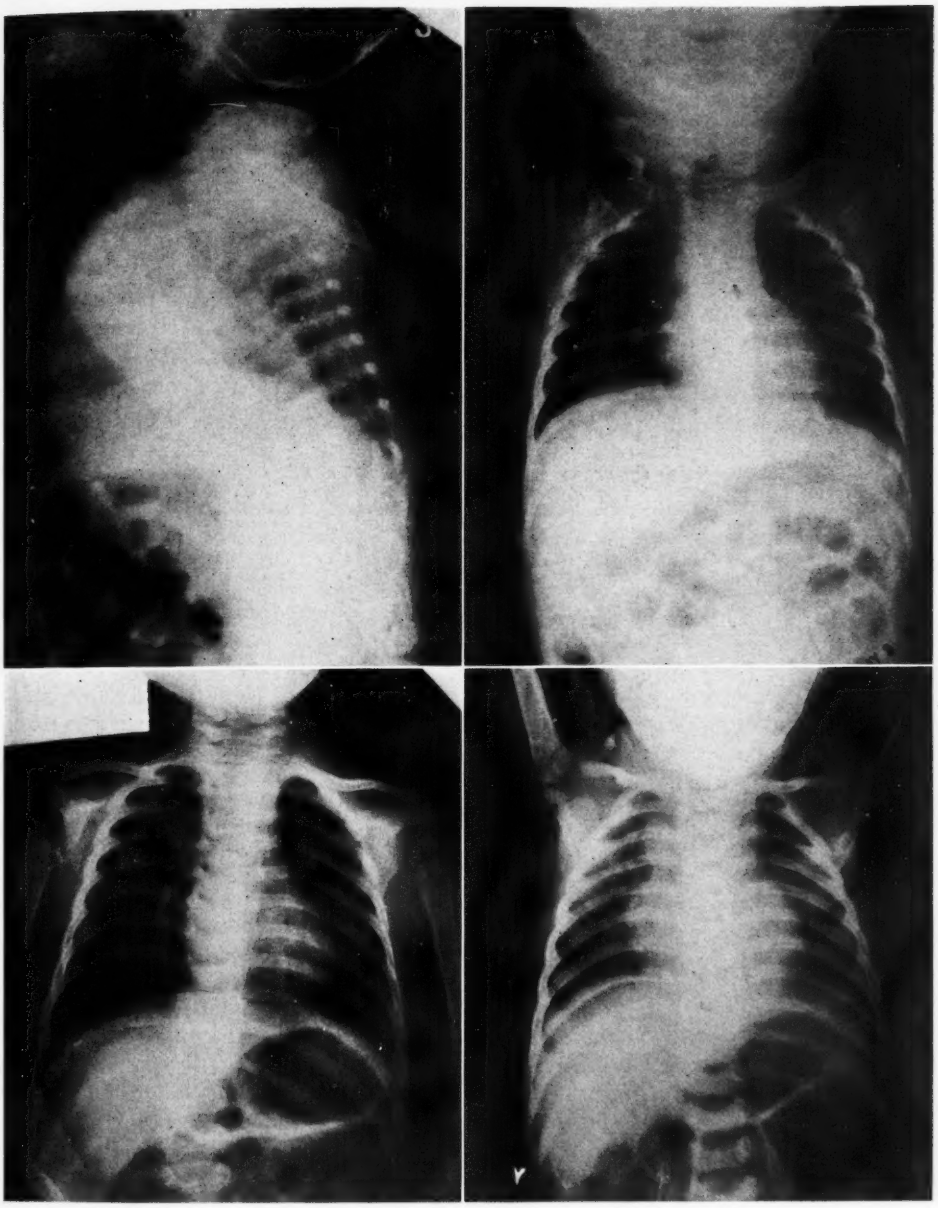

Fig. 4 (*above*). False impression of buckling and compression of the trachea in the lateral view. This is due chiefly to distortion from rotation of the patient and also to the fact that the film was taken during expiration.

Fig. 5 (*below*). Normal thymus with change in width due to respiration. The film on the left was taken at full inspiration and is essentially negative. The film of the same patient on the right was taken at expiration and shows an apparently enlarged thymus. This is entirely a physiological effect, but often leads to a mistaken diagnosis of enlarged thymus.

in a child without definite symptoms, is that a warning signal of possible danger?

REVIEW OF LITERATURE

There is a definite trend, particularly in

Fig. 6. Tuberculous adenitis simulating thymic enlargement. The film on the left shows widening of the superior mediastinal shadow. The film on the right, taken four years later, shows calcification in this region, proving the process to be tuberculous. (*These films used through the courtesy of M. L. Pindell, M.D., Los Angeles.*)

the more recent literature, toward an increasingly doubtful attitude as to the significance of the thymus than that which prevailed a few years ago. Young and Turnbull (6), reporting for the Status Lymphaticus Investigation Committee of Great Britain, concluded: "The facts elicited in the present inquiry afford no evidence that so-called 'Status Thymicolymphaticus' has any existence as a pathological entity."

Hudson (7), presenting information from the Children's Hospital in Boston states that Dr. J. P. Mahoney analyzed the data from the records of 16,195 children anesthetized between Jan. 1, 1930, and Sept. 1, 1934. There were 225 deaths (1.4 per cent) and autopsies were obtained in 70 per cent. He was unable to find a death which could be attributed to the thymus. Hudson concludes, "The evidence does not support the contention that the thymus may be a cause of sudden death in infants and children."

Kennedy and New (8), reporting admissions at the Mayo Clinic extending over a period of ten years, found no death which was attributable to hypertrophy of the thymus, either spontaneously or during or following anesthesia, in a large number of surgical procedures among the newborn and older infants. They conclude that enlargement of the thymus can seldom, if ever, be established as a cause of death.

J. L. Morse (9) says, "There is no proof that the enlargement of the thymus is a primary or causative factor in the pathologic complex described as status lymphaticus."

Wasson (10) has emphasized how infection of sinuses and bronchi produces symptoms which may simulate the stridor, diagnosed as that of enlarged thymus.

Abt (11), of Chicago, in speaking of stridor in children, says, "I do not believe there is any evidence during life or postmortem to show that the thymus enlargement causes enough compression of the trachea, bronchi, or larynx to produce stridor. Every other possibility should be excluded before a diagnosis of stridor due to enlargement of the thymus is made."

Waldbott (12) has shown that a large proportion of cases presenting so-called thymic symptoms have definite allergy, and believes thymic death may be the result of a primary anaphylactic edema of the lungs, with ensuing asphyxiation.

However, there are many others, such as Douglas Symmers (13), with his wide experience in Bellevue Hospital, and Gilkey (14), who find positive evidence of the re-

lation of the thymus to status lymphaticus, and note this condition in 6 to 7 per cent of their autopsies.

REPORT OF CASES

In the midst of these conflicting opinions a review was made of 88 cases, at the Los Angeles County Hospital, that carried a diagnosis of enlarged thymus. These probably do not represent all the cases and any figures given cannot be taken as exact percentage values, but they are sufficient to afford a reliable cross-section of the situation.

Of these 88 cases, 14 were children who had come to autopsy without previous roentgen examination, and the diagnosis of enlarged thymus was part of the autopsy report. It is particularly significant that all of these were cases of sudden death or of death following an acute fulminating illness of very short duration. This is in accordance with the studies of Boyd (15), who has demonstrated that the large prominent thymus and lymph nodes found in cases of sudden death, and which had been mistaken for a pathological state, are really the normal, whereas most thymuses as seen at autopsy are the involuted, inconspicuous thymuses of inanition, which had heretofore been considered normal. She found that when death occurs within from one day to one week of the onset of any disease, the weight of the thymus is moderately reduced; when death occurs one week or more after the onset, the weight is usually markedly reduced, except in persons with exophthalmic goiter or lymphatic leukemia.

The remaining 74 had roentgen examination, and of these, 54 were treated for enlarged thymus. Of the treated cases, nine (17 per cent) appeared to be improved, ten (19 per cent) have no follow-up history and conclusions cannot be drawn as to the effects of the roentgen treatment. Several of those manifesting clinical improvement following roentgen treatment showed no change in the size of the thymus, when roentgenograms were taken from a few weeks to several months later. Thirty-five (65 per cent) had co-existence of other conditions which render it doubtful that thymic enlargement was the real cause of the symptoms. A large number showed complicating otitis media, sinusitis, upper respiratory infection and such conditions as allergy, congenital laryngeal stridor, congenital lues, congenital heart disease, retro-pharyngeal abscess, submaxillary abscess, bronchitis, pneumonia, whooping cough, tuberculous adenitis, prematurity, probable intracranial birth injury, and paresis.

The following are illustrative cases:

Case 1 (Fig. 7). A male infant, aged three months, had been ill for about three weeks with upper respiratory infection, bilateral otitis media, and bronchopneumonia, then developing induration of the posterior pharyngeal wall. Roentgenograms taken at this time showed bulging of the retropharyngeal space probably due to abscess. They also showed broadening of the upper mediastinal silhouette, especially on the right, resembling an enlarged thymus. The symptoms cleared with incision and drainage of the abscess. Roentgen therapy was also given on the suspicion of enlarged thymus, but it is doubtful if any thymic pathology was present.

Case 2 (Fig. 8). This was a five-weeks-old female infant with a history of inspiratory stridor, heavy breathing, and difficulty in swallowing for about three weeks. The films of the chest were essentially negative, but a therapeutic test with roentgen rays was given, without improvement. Later laryngoscopic examination showed congenital laryngeal stridor, which improved with cod liver oil and calcium therapy.

Mention should also be made of the question frequently raised as to possible ill effects from irradiation of the thymus in infants. In 1927, Hess (16) reported two cases of children developing Mongolian idiocy following roentgen treatment. Rowntree (17) and others have recently reported cases which had been subjected to roentgen therapy in early infancy, in which retardation, mentally or physically or both, was later found. Their work, in

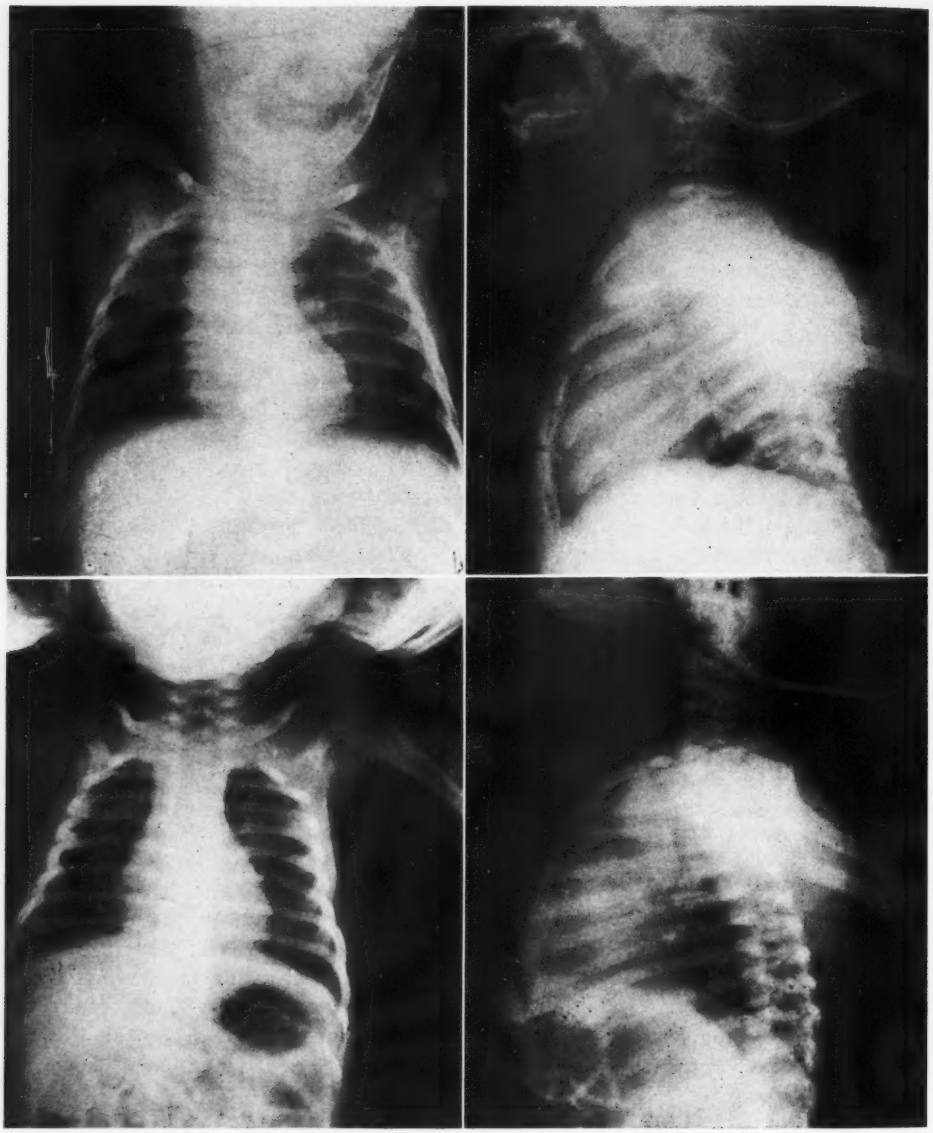

Fig. 7 (*above*). Case 1. Retropharyngeal abscess with suspicion of associated enlarged thymus. The symptoms subsided with incision and drainage of the abscess.
Fig. 8 (*below*). Case 2. Normal chest films. Roentgen treatment given as a therapeutic test, without improvement. Later, laryngoscopic examination revealed congenital laryngeal stridor.

which substitution therapy with injection of thymus extract is employed, will be followed with interest. The function of the gland is still incompletely understood and there is a growing feeling that caution should be exercised in exposing an infant's thymus to the roentgen ray.

CONCLUSIONS

It is evident from the material presented that roentgen diagnosis of thymic enlargement is difficult and requires meticulous care in the examination, due to the ease and frequency with which change in position, varying respiratory phase, and

other factors may give shadows simulating enlarged thymus.

The criteria commonly given for enlarged thymus are unreliable, because of the wide range in size within apparently normal limits. In children meeting sudden death, as from accident, autopsy often reveals thymuses which would be deemed enlarged, although the children had been normal in all respects.

Even in those children presenting symptoms such as are usually attributed to enlarged thymus and in whom roentgen examination shows thymic enlargement, the great majority (65 per cent in the present series) have other causes to account for their symptoms. For this reason thorough pediatric and laryngologic examination should be made before roentgen treatment is instituted.

The propriety of a therapeutic test with roentgen rays for diagnosis must be questioned, chiefly because it may cause cessation of the search for other factors.

In view of our incomplete knowledge of the function of the thymus and because of possible deleterious effects from over-exposure to the roentgen ray, moderate dosage and extreme conservatism should be used in treatment.

Because of the uncertainty accompanying the diagnosis of enlarged thymus and the doubt that the apparently large thymus has any particular significance in symptomless children, we question whether preoperative roentgen examination in children is either necessary or desirable unless specific symptoms or signs are present.

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RADIOLOGICAL SOCIETIES IN THE UNITED STATES

CALENDAR

Meetings Falling between the Dates of May 15 and June 30.

May 20, 21. Pennsylvania Radiological Society at Traylor Hotel, Allentown.

Editor's Note.—Will secretaries of societies please cooperate with the Editor by supplying him with information for this section.

CALIFORNIA

California Medical Association, Section on Radiology.—Chairman, John D. Lawson, M.D., 1306 California State Bldg., Sacramento; *Secretary,* Karl M. Bonoff, M.D., 1930 Wilshire Blvd., Los Angeles. Meets annually with California Medical Association.

Los Angeles County Medical Association, Radiological Section.—President, John F. Chapman, M.D., 65 N. Madison Ave., Pasadena; *Vice-president,* E. N. Liljedahl, M.D., 1241 Shatto St.; *Secretary,* Merl L. Pindell, M.D., 678 South Ferris Ave.; *Treasurer,* Henry Snure, M.D., 1414 Hope Street. Meets every second Wednesday of month at County Society Building.

Pacific Roentgen Club.—Chairman, Raymond G. Taylor, M.D., 1212 Shatto St., Los Angeles; *Secretary,* L. Henry Garland, M.D., 450 Sutter St., San Francisco.

San Francisco Radiological Society.—Secretary, L. H. Garland, M.D., 450 Sutter Street. Meets monthly on first Monday at 7:45 P.M., alternately at Toland Hall and Lane Hall.

COLORADO

Denver Radiological Club.—President, John S. Bouslog, M.D., 246 Metropolitan Bldg.; *Vice-president,* Sanford Withers, M.D., 304 Republic Bldg.; *Secretary,* Ernst A. Schmidt, M.D., Colorado General Hospital; *Treasurer,* H. P. Brandenburg, M.D., 155 Metropolitan Bldg. Meets third Tuesday of each month at homes of members.

CONNECTICUT

Connecticut State Medical Society, Section on Radiology.—Chairman, Kenneth K. Kinney, M.D., 29 North Street, Willimantic; *Vice-chairman,* Francis M. Dunn, M.D., 100 State Street, New London; *Secretary-Treasurer,* Max Climan, M.D., 242 Trumbull St., Hartford. Meetings twice annually in May and September.

DELAWARE

Affiliated with Philadelphia Roentgen Ray Society.

FLORIDA

Florida State Radiological Society.—President, Gerald Raap, M.D., 168 S. E. First St., Miami; *Vice-president,* H. O. Brown, M.D., 404 First Nat'l Bank Bldg., Tampa; *Secretary-Treasurer,* H. B. McEuen, M.D., 126 W. Adams St., Jacksonville.

GEORGIA

Georgia Radiological Society.—President, James J. Clark, M.D., Doctors Bldg., Atlanta; *Vice-president,* William F. Lake, M. D., Medical Arts Bldg., Atlanta; *Secretary-Treasurer,* Robert C. Pendergrass, M.D., Prather Clinic, Americus. Meetings twice annually, in November and at the annual meeting of the Medical Association of Georgia in the spring.

ILLINOIS

Chicago Roentgen Society.—President, David S. Beilin, M.D., 411 Garfield Ave.; *Vice-president,* Chester J. Challenger, M.D., 3117 Logan Blvd.; *Secretary-Treasurer,* Roe J. Maier, M.D., 7752 Halsted St. Meets second Thursday of each month, September to May, except December.

Illinois Radiological Society.—President, Cesare Gianturco, M.D., 602 W. University Ave., Urbana; *Vice-president,* Fred H. Decker, M.D., 802-Peoria Life Bldg., Peoria; *Secretary-Treasurer,* Edmund P. Halley, M.D., 968 Citizens Bldg., Decatur. Meetings quarterly by announcement.

Illinois State Medical Society, Section of Radiology.—President, Roswell T. Pettit, M.D., 728 Columbus St., Ottawa; *Secretary,* Ralph G. Willy, M.D., 1138 N. Leavitt St., Chicago.

INDIANA

Indiana Roentgen Society.—President, J. N. Collins, M.D., 23 E. Ohio St., Indianapolis; *President-elect,* Stanley Clark, M.D., 108 N. Main St., South Bend; *Vice-president,* Juan Rodriguez, M.D., 2903 Fairfield Ave., Fort Wayne; *Secretary-Treasurer,* Clifford C. Taylor, M.D., 23 E. Ohio St., Indianapolis. Annual meeting in May.

IOWA

The Iowa X-ray Club.—Holds luncheon and business meeting during annual session of Iowa State Medical Society.

MAINE

See New England Roentgen Ray Society.

MARYLAND

Baltimore City Medical Society, Radiological Section.—Chairman, Marcus Ostro, M.D., 1810 Eutaw Place; *Secretary,* H. E. Wright, M.D., 101 W. Read St., Baltimore. Meetings second Tuesday of each month.

MASSACHUSETTS

See New England Roentgen Ray Society.

MICHIGAN

Detroit X-ray and Radium Society.—President, E. W. Hall, M.D., 10 Peterboro Street; *Vice-president,*

Sam W. Donaldson, M.D., 326 North Ingalls St., Ann Arbor; *Secretary-Treasurer*, E. R. Witwer, M.D., Harper Hospital. Meetings first Thursday of each month from October to May, inclusive, at Wayne County Medical Society Bldg.

Michigan Association of Roentgenologists.—President, E. R. Witwer, M.D., Harper Hospital, Detroit; *Vice-president*, D. W. Patterson, M.D., 622 Huron Street, Port Huron; *Secretary-Treasurer*, C. K. Hasley, M.D., 1429 David Whitney Bldg., Detroit.

MINNESOTA

Minnesota Radiological Society.—President, Walter H. Ude, M.D., 78 S. 9th St., Minneapolis; *Vice-president*, Leo G. Rigler, M.D., University Hospitals, Minneapolis; *Secretary-Treasurer*, Harry Weber, M.D., 102 Second Ave., S. W., Rochester. Meetings quarterly.

MISSOURI

The Kansas City Radiological Society.—President, L. G. Allen, M.D., 907 N. 7th St., Kansas City, Mo.; *Secretary*, Ira H. Lockwood, M.D., 306 E. 12th St., Kansas City, Mo. Meetings last Thursday of each month.

The St. Louis Society of Radiologists.—President, Joseph C. Peden, M.D., 634 N. Grand Blvd.; *Secretary*, W. K. Mueller, M.D., 607 N. Grand Blvd. Meetings fourth Wednesday of each month.

NEBRASKA

Nebraska Radiological Society.—President, E. W. Rowe, M.D., 128 N. 13th St., Lincoln; *Secretary*, D. Arnold Dowell, M.D., 117 S. 17th St., Omaha. Meetings first Wednesday of each month at 6 P.M. in Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY

(Maine, New Hampshire, Vermont, Massachusetts, and Rhode Island.) *President*, Frank E. Wheatley, M.D., 520 Beacon St., Boston; *Secretary*, E. C. Vogt, M.D., 300 Longwood Ave., Boston. Meetings third Friday of each month from October to May, inclusive, usually at Boston Medical Library.

NEW HAMPSHIRE

See New England Roentgen Ray Society.

NEW JERSEY

Radiological Society of New Jersey.—President, J. D. Tidaback, M.D., 382 Springfield, Summit; *Vice-president*, Milton Friedman, M.D., Newark Beth Israel Hospital, Newark; *Secretary*, P. S. Avery, M.D., 546 Central Ave., Bound Brook. Meetings at Atlantic City at time of State Medical Society, and Midwinter in Newark as called by president.

NEW YORK

Brooklyn Roentgen Society.—President, Albert Voltz, M.D., 115–120 Myrtle Avenue, Richmond Hill; *Vice-president*, A. L. L. Bell, M.D., Long Island College Hospital, Henry, Pacific, and Amity Sts., Brooklyn; *Secretary-Treasurer*, E. Mendelson, M.D., 132 Parkside Ave., Brooklyn. Meetings first Tuesday in each month at place designated by president.

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Long Island Radiological Society.—President, David E. Ehrlich, M.D., 27 W. 86th St., New York City; *Vice-president*, H. Koiransky, M.D., 43–37 47th St., Long Island City; *Secretary*, S. Schenck, M.D., 115 Eastern Parkway, Brooklyn; *Treasurer*, Moses Goodman, M.D., 45–01 Skillman Ave., Long Island City. Meetings fourth Thursday evening each month at Kings County Medical Bldg.

New York Roentgen Society.—President, E. F. Merrill, M.D., 30 W. 59th St., New York City; *Vice-president*, I. W. Lewis, M.D.; *Secretary*, H. K. Taylor, M.D., 667 Madison Ave., New York City; *Treasurer*, R. D. Duckworth, M.D., 170 Maple Ave., White Plains. Meetings third Monday evening each month at Academy of Medicine.

Rochester Roentgen-ray Society.—Chairman, Joseph H. Green, M.D., 277 Alexander St.; *Secretary*, S. C. Davidson, M.D., 277 Alexander St. Meetings at convenience of committee.

Society of Radiological Economics of New York.—President, Albert L. Voltz, M.D., 115–120 Myrtle Ave., Richmond Hill; *Vice-president*, M. M. Pomeranz, M.D., 911 Park Ave., New York City; *Secretary*, W. F. Francis, M.D.; *Treasurer*, Theodore West, M.D., United Hospital, Port Chester. Meetings first Monday evening each month at McAlpin Hotel.

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Radiological Society of North Carolina.—President, Robert P. Noble, M.D., 127 W. Hargett St., Raleigh; *Vice-president*, A. L. Daughtridge, M.D., 144 Coast Line St., Rocky Mount; *Secretary-Treasurer*, Major I. Fleming, M.D., 404 Falls Road, Rocky Mount. Meetings with State meeting in May, and meeting in October.

OHIO

Cleveland Radiological Society.—President, North W. Shetter, M.D., Lakewood City Hospital, Lakewood; *Vice-president*, John Heberding, M.D., St. Eliza-

beth's Hospital, Youngstown; *Secretary-Treasurer*, Harry Hauser, M.D., Cleveland City Hospital, Cleveland. Meetings at 6:30 P.M. at Cleveland Chamber of Commerce Club on fourth Monday of each month from October to April, inclusive.

Radiological Society of the Academy of Medicine (Cincinnati Roentgenologists).—*President*, George Benzing, M.D., St. Elizabeth Hospital, Covington, Ky.; *Secretary-Treasurer*, Justin E. McCarthy, M.D., 707 Race St., Cincinnati, Ohio. Meetings held third Tuesday of each month.

PENNSYLVANIA

Pennsylvania Radiological Society.—President, Sydney J. Hawley, M.D., Geisinger Memorial Hospital, Danville; *First Vice-president*, William J. McGregor, M.D., 744 Franklin Ave., Wilkinsburg; *Second Vice-president*, Oscar M. Weaver, M.D., 12 S. Main St., Lewistown; *Secretary-Treasurer*, Lloyd E. Wurster, M.D., 416 Pine St., Williamsport; *President-elect*, Charles S. Caldwell, M.D., 520 S. Aiken Ave., Pittsburgh. Annual meeting, May, 1938. Exact date and place to be decided.

Philadelphia Roentgen Ray Society.—President, Thomas P. Laughery, M.D., Germantown Hospital; *Vice-president*, Elwood E. Downs, M.D., Jeans Hospital, Fox Chase; *Secretary*, Barton H. Young, M.D., Temple University Hospital; *Treasurer*, R. Manges Smith, M.D., Jefferson Hospital. Meetings first Thursday of each month from October to May, Thompson Hall, College of Physicians, 19 S. 22nd St., 8:15 P.M.

The Pittsburgh Roentgen Society.—President, F. L. Schumacher, M.D., Jenkins Arcade; *Secretary*, H. N. Mawhinney, M.D., Mercy Hospital. Two Fall and two Spring meetings at time and place designated by president.

RHODE ISLAND

See New England Roentgen Ray Society.

SOUTH CAROLINA

South Carolina X-ray Society.—President, Robert B. Taft, M.D., 105 Rutledge Ave., Charleston; *Secretary-Treasurer*, Hillyer Rudisill, M.D., Roper Hospital, Charleston. Meetings in Charleston on first Thursday in November, also at time and place of South Carolina State Medical Association.

SOUTH DAKOTA

Meets with Minnesota Radiological Society.

TENNESSEE

Memphis Roentgen Club.—Chairmanship rotates monthly in alphabetical order. Meetings second Tuesday of each month at University Center.

Tennessee State Radiological Society.—President, H. S. Shoulders, M.D., 246 Doctors Bldg., Nashville; *Vice-president*, S. S. Marchbanks, M.D., 508 Medical Arts Bldg., Chattanooga; *Secretary-Treasurer*, Franklin B. Bogart, M.D., 311 Medical Arts Bldg., Chattanooga. Meeting annually with State Medical Society in April.

TEXAS

Texas Radiological Society.—President, R. G. Giles, M.D., Medical Arts Bldg., San Antonio; *President-elect*, Jerome H. Smith, M.D., Shannon West Texas Memorial Hospital, San Angelo; *First Vice-president*, C. F. Crain, M.D., 416 Chaparral St., Corpus Christi; *Second Vice-president*, M. H. Glover, M.D., 904 8th St., Wichita Falls; *Secretary-Treasurer*, G. D. Carlson, M.D., 3121 Bryan St., Dallas. Meets annually. San Antonio is place of meeting, Oct. 22, 1938.

VERMONT

See New England Roentgen Ray Society.

VIRGINIA

Radiological Society of Virginia.—President, Fred M. Hodges, M.D., 100 W. Franklin St., Richmond; *Vice-president*, L. F. Magruder, M.D., Raleigh and College Aves., Norfolk; *Secretary*, V. W. Archer, M.D., University of Virginia Hospital, Charlottesville.

WASHINGTON

Washington State Radiological Society.—President, H. E. Nichols, M.D., Stimson Bldg., Seattle; *Secretary*, T. T. Dawson, M.D., Fourth and Pike Bldg., Seattle. Meetings fourth Monday of each month at College Club.

WISCONSIN

Milwaukee Roentgen Ray Society.—Secretary, S. A. Morton, M.D., Columbia Hospital, Milwaukee. Meets monthly on first Friday.

Radiological Section of the Wisconsin State Medical Society.—Secretary, Russel F. Wilson, M.D., Beloit Municipal Hospital, Beloit. Two-day annual meeting in May and one day in connection with annual meeting of State Medical Society, in September.

University of Wisconsin Radiological Conference.—Secretary, E. A. Pohle, M.D., 1300 University Ave., Madison, Wis. Meets every Thursday from 4 to 5 P.M., Room 301, Service Memorial Institute.

EDITORIAL

LEON J. MENVILLE, M.D., *Editor* HOWARD P. DOUB, M.D., *Associate Editor*

THE POSITION OF RADIOLOGY IN EXPANDING MEDICAL SCIENCE[1]

The citizens of the United States feel highly honored that our country has been chosen as the meeting place for 1937 of the International Congress of Radiology, an association recognized by civilized countries of the world for its achievements in advancing the social well-being of all peoples.

In this war-torn world, it is gratifying to remember that science has no country, to know that men of science from all parts of the universe, of whatever nationality, race, or creed they may be, can meet and freely discuss contributions to the welfare of mankind. Let us hope that out of such peaceful international gatherings as this, some impetus to world peace may come.

The contributions of radiology to the health and happiness of man and to social progress have been one of the wonders of our generation. Radiology has given an understanding of the intricate physical processes of health which are almost beyond the scope of the imagination, and has made possible the accurate location and diagnosis of disease in the human body.

Man's brain is the visual brain of the primates. It is true that there are other primates besides man, but they have achieved no result with the visual brain which has advanced them beyond the lower animals with the predominantly olfactory brain. In his physical make-up, man in comparison with many of the lower animals is inferior and his lifetime on earth is measured by a relatively small number of years, but his brain has given him superiority over all other animals, and the eye is the organ through which man receives his truest knowledge. It is the fact that the mind of man was built up coincidentally with the eye, and not the mechanics of the eye, that has made his intellectual progress possible. The outstanding fact in the history of medicine is that the visual method of obtaining information has always been dominant. Radiology has been a powerful factor in extending the visual method.

[1] Opening Address at Fifth International Congress of Radiology, Chicago, Sept. 13–17, 1937.

It might be said that what Hippocrates was to Aristotle, Harvey was to Sydenham, the great clinician (1624–1689). The observations of Hippocrates in clinical medicine furnished, in the succeeding century, a foundation for the monumental work of Aristotle in the basic sciences, as the discoveries of Harvey inspired Sydenham, "the English Hippocrates," and his contemporaries to reject dogmas and make clinical application of knowledge gained by observation.

If we review medical history from the time of Aristotle (384–322 B.C.) to the discovery of the microscope, we find that in the many centuries of the Dark Ages little progress was made in the medical sciences, although some knowledge of anatomy and physiology and clinical symptomatology was recorded. The compound microscope, the earliest crude form of which was introduced by the Jannsens about 1590, was the most significant contribution of all time, which was to revolutionize medicine and change the history of mankind. This instrument opened a new scientific world and enabled the student to recognize the body tissues in health and in disease.

While the discovery of the microscope came too late to aid Harvey (1578–1657) greatly in his demonstration of the circulation of the blood, it gave a crude magnifying instrument to William Hunter (1718–1783) and John Hunter (1729–1793) and the modern microscope to Pasteur and Lister. The microscope in a relatively few years extended the breadth and the depth of understanding and developed a new anatomy of the minute and the new physiology which went with it.

With the aid of the imperfect microscope, the two brothers, William and John Hunter, co-ordinated knowledge in anatomy, physiology, and pathology so that for the first time these basic sciences became a coherent whole and medicine was placed on a sound foundation. The greatest single contribution of the Hunters was the discovery of the lymphatic system, as related to the organs and tissues of the body,

which in many respects was as far-reaching as the discovery of the circulation of the blood. By the aid of the microscope they were able to follow the course of injections of dyes into vascular and lymph channels, a method which was introduced by Belchier of Guy's Hospital in 1764, knowledge which has been astonishingly utilized by diagnostic radiology in the demonstration of the circulation in health and disease.

Contemporary with the Hunters was Edward Jenner (1749–1823) from whose work the whole fabric of preventive medicine and immunization was brought into existence. And here again radiology has carried the sense of sight to new heights of understanding of the fundamental conception of the etiology of disease and its prevention.

Early in the nineteenth century came evidence of growing interest in histology. Schneiden and Schwann, in 1838, first described the cell, which Virchow said was the unit of life. And from Virchow and his school, through the cell theory, came a newer and better understanding of anatomy and physiology which he called "cellular pathology." The greater part of this new knowledge came from the study of material obtained at necropsy. However, while dead-house pathology gave an enormous amount of knowledge, it did not lead to rapid improvement in therapeusis. The physical changes resulting from terminal causes such as infections so often obscured the early disease manifestations that postmortem study gave too little understanding of the disease in its curable stages. Interpretation of the pathology of the living is the outstanding feature of modern medicine and in this field diagnostic radiology has been of incomparable service in carrying sight into the unseen spaces of the living body.

A hundred years after the Hunters, there were born two men, Pasteur (1822–1895), and Lister (1827–1912), through whom medicine was reborn. With improved microscopes and staining and cultural methods, Pasteur, of France, proved his theory of the origin of disease in micro-organisms, and changed the entire aspect of medicine. Lister, of England, related micro-organisms to infections and putrefactive processes; hospitals for the first time became safe, and modern surgery developed. Here again radiology has been the agent which has brought to the light the early manifestations of disease in concealed situations while in a curable stage.

In 1882, Koch, with cultural methods and the microscope, made his demonstration of the bacillus of tuberculosis. The disease tuberculosis had been one of the major causes of death of man, and it was learned from Koch's discovery, what had been suspected, that tuberculosis was not a hereditary disease, but that it was essentially contagious, that it was a disease of the lower animals as well as of man, although manifesting itself by attacking tissues not commonly involved in man.

Not until the twentieth century was the cause of syphilis determined, by Schaudinn, in 1905. Syphilis had existed from ancient times, and as the result of travel and admixture of peoples it spread over the world. With the scientific demonstration of the *Spirochaeta pallida*, medicine again advanced in its work of stamping out disease and prolonging the life of man. To-day, radiology, which demonstrates so readily the specific characteristics of these two great plagues, gives new knowledge of tuberculosis and syphilis.

But radiology has gone further: it has entered the field of physics and chemistry.

Radiology came from the development of the minute beyond the power of the microscope to reveal, and developed methods whereby not only the cell was broken up into atoms, but finally the atom itself was divided into its component parts. Information of enormous scientific importance had been developing since the work of John Mayow (1643–1679), of whom we have heard too little, one of the first of the physician-chemists. The observations and experiments of Mayow led later to the discovery of oxygen, and to-day, after nearly three hundred years, we are just beginning to understand those fundamental problems which connect physiochemistry with the medical sciences.

Brown, the English botanist, had long been making the observations in physics which culminated in his written communications of 1827. At about this period John Dalton was working on the atomic theory and the constitution of the molecule. Thomas Graham, Master of the Mint in London, in 1861 published his observations, which led to the first great description of colloid bodies. Tyndall called attention to the curious phenomenon occurring in the track of a luminous beam, the colorings of which are the effect of sunlight on colloids in the air, and investigated the transparency and opacity of gases and vapors under radiant heat,

a new conception of invisible rays almost beyond the comprehension of man.

And now came the phenomenal discoveries, by most convincing original work, to which the world owes a debt of gratitude. Crookes (1832–1919) was the last of the great all-round physicists. He gave the fundamental knowledge of the cathode rays, the basic conception of the x-rays. Roentgen was working with Crookes' tubes when he discovered the x-rays, in 1895. The Curies discovered radium in 1898. Through the application of the x-rays and radium, knowledge of radiology was advanced with extraordinary speed, all the related sciences of medicine and of surgery progressed rapidly with the aid of the new instruments of precision connected with radiology, and by means of new forms of photography, ultramicroscopic phenomena were made visible to the eye.

Because of the extraordinary development which has come from radiology, we not only are able to bring knowledge to the brain of man, but have learned that the x-rays, beta rays, and gamma rays have an enormous and growing therapeutic value. New rays of vast extent of which we are just beginning to be conscious are demonstrated, and there is developing an entirely new theory of rays which in its scope and complexity appeals to the mind of man and opens a new understanding of science. As a result, medicine and surgery find themselves fortified by relatively new agents which day by day are being used increasingly in the treatment of disease. We recognize that in certain situations advanced cancer, which is beyond reasonable possibility of cure by the knife, can with but little risk be treated with radiant energy in the form of x-rays and radium, and even cured, if it has not progressed beyond the immediate site. We find that certain cellular tumors which are extremely active in growth can be treated with radiology with better results than with surgery, and without serious risk. This new agent, which began as an aid to surgery and medicine, extends its usefulness day by day.

From the period of the unaided eye, through the era of the development of the microscope and its revolution of scientific medicine, we have entered, through radiology, into another epoch of scientific achievement not only in medicine and in the allied fields, but in universal science.

Let us think for a moment of the science of astronomy, which challenges the imagination of man, unbelievable were it not that it proves the correctness of its premises. Just as the microscope and radiology have carried knowledge into the minute, so have the giant telescopes carried the eye into the heavens. Let us be thankful that power has been given to the brain of man through the eye to understand and appreciate these extraordinary discoveries, for the two closely related manifestations of radiant energy, radiology and astronomy, have been brought through photography within the comprehension of all the people, the layman as well as the scientist.

In the name of organized medicine, I bid you welcome to the United States, and I pay homage to science, in which radiology is establishing a new leadership.

WILLIAM J. MAYO, M.D.
Rochester, Minn.

ANNOUNCEMENTS

NEXT ANNUAL MEETING

The next Annual Meeting of the Radiological Society of North America will be held at Pittsburgh, Pa., at the Hotel William Penn, November 27–December 2, 1938.

CHICAGO TUMOR INSTITUTE

March 21, 1938, marked the opening of the Chicago Tumor Institute which will offer consultation service to physicians in the diagnosis and treatment of cancer, and radiation facilities for cancer patients. The Institute is a corporation not for profit which proposes to conduct research and to offer training to physicians who may wish to qualify as specialists in the study and treatment of cancer.

The Board of Trustees is as follows: Ludvig Hektoen, M.D., *President;* Arthur H. Compton, Ph.D., *Vice-president;* Roy G. Osgood, *Treasurer;* M. J. Spiegel, Mrs. Francis Neilson, Mrs. Arthur Meeker, Alfred Busiel, and Max Cutler, M.D.

The Scientific Committee is composed of the following members: Max Cutler, M.D., *Director;* Sir G. Lenthal Cheatle, F.R.C.S., of London; Henri Coutard, M.D., formerly of Paris, France; Arthur H. Compton, Ph.D., of the University of Chicago, winner of the 1927 No-

bel Prize in Physics, and Ludvig Hektoen, M.D., of the American Medical Association.

The Institute is located at 21 West Elm Street, Chicago. Mr. Walter W. Stevens is Administrative Officer.

INDUSTRIAL RESEARCH LABORATORIES

Revision of Bulletin 91, National Research Council

The increase in the number of research laboratories maintained by industrial concerns in the United States during the last few years has made it seem desirable to issue a new edition of the National Research Council's Bulletin, "Industrial Research Laboratories of the United States," fifth edition.

On March 25, questionnaires were mailed to the 1,562 concerns which were included in the last edition of 1933, and to a large number of new concerns which are thought to maintain laboratories.

If the reader of this note is a member of a firm which maintains a laboratory where research looking toward the development and improvement of products is carried on, it is hoped that he will ascertain whether a questionnaire has been received by his company, and if not, that he will request one from the Library, National Research Council, 2101 Constitution Avenue, Washington, D. C.

There is no charge for the entry in the bulletin, the only requirement being that the laboratory is undertaking research.

It is desirable to have the information for the bulletin in hand as soon as possible so that the publication may appear within the current year.

NOTE OF CORRECTION

The Editor wishes to call attention to an error in the caption of the cut on page 510 of the April issue of RADIOLOGY in which Dr. W. Edward Chamberlain is mistakenly named as Chairman of the American Board of Radiology. He is, as is well known, Chairman of the Board of Chancellors of the American College of Radiology. Dr. B. R. Kirklin is Secretary of the American Board of Radiology.

IN MEMORIAM

SANFORD WITHERS, M.D.

1891–1938

Sanford Withers, the son of George A. and Avis Martin Withers, was born in Clearwater, Wayne County, Missouri, Nov. 25, 1891. He received his primary school education in Piedmont, Missouri, and Lincoln, Nebraska, and his high school education at Manual Training High School in Kansas City, Missouri. He graduated from there in 1910, one of the two boys to receive scholarships in engineering and architecture for Washington University, St. Louis. There may be some prophetic significance in the fact that he was one of the members of the senior class of Manual Training High School which, in 1910, helped build an x-ray machine.

As the scholarship was not sufficient to cover his expenses at college, Sanford Withers delayed accepting it until 1912. In the meantime (1910–1911), to earn money enough to permit his attending college, he worked as assistant city chemist for Kansas City, Missouri. He entered Washington University in 1912 and continued his studies there, with chemical engineering as his goal, until some time during his third year, when he decided to go into medicine. His medical course was interrupted in 1917 by his entrance into service for the World War. He was a student with United States Base Hospital Unit No. 21 from May 12, 1917, to March 19, 1919.

After his discharge, he returned to Washington University and received his degree of Doctor of Medicine there in 1919. He was at the Barnard Free Skin and Cancer Hospital, St. Louis, Missouri, from March, 1919, to July 1, 1920, as an interne; then as resident from July 1, 1919, to July 1, 1920, and as associate physician from July 1, 1920, to November, 1921. While in St. Louis, Dr. Withers was a member of Chi Zeta Chi medical fraternity (now Phi Rho Sigma) and the University Club. From June, 1920, until November, 1921, he practised dermatology in St. Louis.

He moved to Denver in 1921 and that year was licensed to practise medicine there and was consultant for the Radium Company of Colo-

rado from November, 1921, to July, 1923. In January, 1924, he married Matilda Branstetter. They had two children: Jane, born in November, 1926, and Guy, born in January, 1928.

In Denver, Dr. Withers limited his practice to radiology. He served as Radiologist to the Denver General Hospital from 1926, and as Radiation Therapist to Beth Isreal Hospital, Denver, from 1928. Beside his hospital duties and his private practice in the years succeeding 1922, he conducted private courses in the use of radium and x-ray in the treatment of neoplastic diseases. Over 300 physicians took these courses. To equip himself to teach, beside his previous training and constant study, he had taken a course at the New York State Institute for the Study of Malignant Diseases and had visited all the centers for the treatment of malignant disease in the United States.

In September, 1937, Dr. Withers installed 400,000-volt roentgen therapeutic equipment, and in October he began to notice evidence of aplastic anemia. This became progressively worse in spite of remedial and therapeutic care, and shortly after the first of the year, 1938, he went to New York City. He died there on March 8, 1938, of aplastic anemia with a terminal bronchopneumonia.

The late Sanford Withers, M.D., long an honored member of the Radiological Society of North America.

Dr. Withers was a member of the staff of Mercy Hospital (Denver), Presbyterian Hospital (Denver), St. Luke's Hospital (Denver),

St. Joseph's Hospital (Denver); of the American Medical Association, the Denver County and Colorado State Medical Societies, the Radiological Society of North America, the American Radium Society, the American Society for the Control of Cancer, the American Board of Radiology, the American College of Physicians, the American College of Radiology, the Denver Radiological Club, the Denver Public Health Council, the British Institute of Radiology, the Roentgen Society of London, Rouen Post of the American Legion (St. Louis), and the Emulation Masonic Lodge (Denver). He was President of the American Radium Society, 1932–1933, and at the time of his death he was Chairman of the Colorado Committee for the American Society for the Control of Cancer, and Chairman of the Committee on Cancer Education of the Colorado State Medical Society. The bibliography of Dr. Withers' publications reveals that they dealt amost entirely with the treatment of tumors and malignancies and were published in many journals.

These are the bare statements concerning Dr. Withers' professional attainments. Nothing has been said about his love for his family and for the great outdoors. Only those who have been fortunate enough to have been with him on his various hunting and fishing trips could really know him as a companion and friend. For many years, he was afflicted with exophthalmic goiter, but in spite of poor health he carried on and was always interested in public health and the advancement of radiology

W. W. Wasson, M.D.

BOOK RECEIVED

Books received are acknowledged under this heading, and such notice may be regarded as an acknowledgement of the courtesy of the sender. Reviews will be published in the interest of our readers and as space permits.

Le Diagnostic Radiologique des Tumeurs Malignes du Pharynx et due Larynx (The Radiologic Diagnosis of Malignant Tumors of the Pharynx and Larynx). An Anatomo-topographic and radiographic study. By Dr. F. Baclesse, Head of the Service at the Curie Foundation (Institute of Radium at the University of Paris). Preface by Dr. A. Hautant. A volume of 270 pages, with 236 figures. Published by Masson et Cie, Paris, 1938. Price: 100 fr.

BOOK REVIEW

Einführung in die Kurzwellentherapie Behandlungstechnik und Indikationen (Introduction to the Technic and Indications of Short Wave Therapy). By Dr. Ernst Fritsch and Dr. Martin Schubart, of Berlin, in collaboration with Dr. W. Gutsch, of Berlin, with an introduction by Dr. A. Esau. A volume of 200 pages, with 178 illustrations. Published by Urban & Schwarzenberg, Berlin, 1938. Price: rm. 5.50.

This introduction to short wave therapy is well prepared and illustrated. There are chapters on general considerations, physical principles, technic of short wave production and short wave apparatus, the physical differentiations between the tube apparatus and the spark gap apparatus, estimation of the performance of short wave apparatus, the electrodes, the foundations of treatment technic, biologic and therapeutic efficacy of short waves, treatment technic with short wave therapy in various diseases, short wave therapy in the treatment of eye diseases, the production of artificial fevers with short waves (electropyrexia, and short wave hyperthermia), and end-results. There is appended a good bibliography, particularly of the German and French literature on the subject. The authors recommend chiefly the use of the electrostatic field and, although they do discuss the use of the electromagnetic field, they give insufficient data on this phase of the subject. The book can be recommended to all physicians interested in short wave diathermy.

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ABNORMALITIES

Anomalies of the Ribs in Childhood. Stefan Simon. Röntgenpraxis, January, 1938, **10,** 45–50.

Since roentgenograms of the chest have been used more or less routinely for the diagnosis of diseases of the lung in children, anomalies of the ribs have been found rather frequently. They may be demonstrated in from 2 to 3 per cent of all children. They consist mostly of bony bridges between two ribs, of a fork-like deformity of their anterior ends, or of anomalous bony processes at some point of the ribs.

HANS W. HEFKE, M.D.

ANIMAL EXPERIMENTATION

The Histological Changes in the Infectious Papilloma of the Rabbit during the Healing Stage Following Roentgen Irradiation. A. Lacassagne. Strahlentherapie, 1937, **60,** 290.

The infectious papilloma of the rabbit was discovered by R. E. Shope, in 1933, and has been used since for radiobiological investigations. The author studied its response to roentgen rays (180 kv., 5 ma., 30 cm. F.S.D., 1 mm. Cu + 3 mm. Al, 12 cm.^{2} field size; exposure for one and one-half hours; dose 3,000 r). The infectious papilloma healed completely in a few days following this treatment. It appeared that the abnormal epithelial cells show a higher susceptibility to irradiation than the normal cells of the epidermis from which they originate. The reparative process is very similar to that observed by the author in irradiated epithelioma in man.

ERNST A. POHLE, M.D., Ph.D.

APPARATUS

The Reconstruction of Anatomical Planes by Means of Radiography: The "Biotome" and "Phototome" of Bocage. Delherm and Ch. Proux. Bull. et mém. Soc. de Radiol. méd. de France, October, 1937, **25,** 608–611.

The authors discuss the various methods of planigraphy and the problem of radioscopy of a plane, giving credit to Bocage for his work in these fields. Brief descriptions of a new apparatus for fluoroscopy and of one for radiography of images in one plane are given.

S. R. BEATTY, M.D.

Radioscopy of a Plane of the Body: Its Value and Practical Realization. P. Ponthus. Bull. et mém. Soc. de Radiol. méd. de France, October, 1937, **25,** 603–608.

The author describes a method for radioscopic visualization of a single plane of the body which he has found experimentally practical. The method depends on the synchronization of a circular movement of the tube and of an optical system of two mirrors, at 45° angles to the screen, which scan the moving image on the fluorescent screen and produce the illusion of a stationary image of a single plane of the body. The center of the optical system is fixed to rotate about the axis of rotation of the tube. The author states that in selecting a given plane the experimental apparatus is accurate to within 5 mm. There are certain advantages to radioscopic planigraphy over radiologic methods, particularly in that the chosen plane can be easily selected. The method would be of considerable value also as an adjunct to radiologic methods in selecting the levels of the planes to be studied.

S. R. BEATTY, M.D.

Stratigraphy of the Lung by the Method of Vallebona: Presentation of an Apparatus for Stratigraphy, the Oscillo-strator. G. Ronneaux and J. M. Lemoine. Bull. et mém. Soc. de Radiol. méd. de France, October, 1937, **25,** 592–599.

The authors present their apparatus for stratigraphy of the chest built according to the principle suggested by Vallebona. The tube is fixed at a distance of 1 meter and 90 cm. The film and the patient are rotated simultaneously through 20–30° of an arc during exposure. The authors obtained results equal to those obtained by other methods of planigraphy in use and they believe that their method has the advantage of simplicity. The apparatus is described in some detail.

S. R. BEATTY, M.D.

The Problem of Roentgen Dosage by Means of Photometry of Fluorescent Screens. A. Langer and J. Sprindrich. Strahlentherapie, 1937, **59,** 680.

The authors discuss the use of fluorescent screens in roentgen-ray dosimetry, a principle which was used first by Wintz and Rump. In connection with a photoelectric cell of special construction this method may have promising possibilities.

ERNST A. POHLE, M.D., Ph.D.

ARTHRITIS

So-called Arthritis Mutilans. J. Schüller. München. med. Wchnschr., Aug. 27, 1937, **55,** 1381–1386.

An excellent review of the present status of this entity is presented, and six cases are reported. The diagnosis is readily established roentgenographically, and the etiology is amply discussed. This condition is not uncommonly observed in association with psoriasis, and may actually precede the manifestations of psoriasis a few years. When psoriasis is considered the etiologic factor, then the appellation "arthropathia psoriatica" is appropriate. There are different forms, varying from simulants of infectious arthritis, peri-arthritis endocrina destruens, to osteo-arthritis deformans. It is not unusual for a concomitant history of "rheumatic pain" to be present in the early stage of development. The author is strongly of the opinion that mono- or polyarthritis mutilans is definitely resultant of a neurologic lesion, even though a myelodysplasia may not be demonstrable. One case is mentioned in which both the symptomatology and roentgen findings strongly simu-

lated tabes dorsalis. It is difficult to distinguish between them, and indeed it is very likely that the arthropathy resulting from tabes dorsalis, syringomyelia, and spina bifida are similar entities. In the series, two cases were spina bifida, two myelodysplasia, and the remaining two presented vague but not definitely diagnosable neurologic symptoms. Numerous terms have been applied by other authors to lesions presenting very similar signs and symptoms, and probably all these should be included under one terminology, *viz.*, Kienböck called the foot lesions "trophopathia myelodysplastica," Blum considered these lesions as "osteoarthropathia micro-atrophicans," and more recently they have been called "Stursberg's polyarthritis mutilans."

WILLIAM R. STECHER, M.D.

Roentgen Therapy in Acute Para-arthritis. Alfred A. de Lorimier. Am. Jour. Roentgenol. and Rad. Ther., July, 1937, **38,** 178–195.

In cases manifesting aches or neuralgic pain which are concerned with the motion of a joint in the extremities, a localized inflammation of the tendons of one or more muscles within a sector of the joint periphery must be considered. This the author calls "para-arthritis" and includes involvements of the bursa. The shoulder, elbow, hand, hip, knee, foot, or any joint may be involved. Under this heading fall the so-called bursitis, tendonitis, Pellegrini-Stieda's disease, etc.

Most of these cases present symptoms out of proportion to the findings, especially pain, point tenderness, and impaired motion, and roentgenologically, a calcareous deposit. Although trauma is a factor, a large percentage gave no history of it and, therefore, a toxic condition must be considered.

In the acute cases roentgen therapy produces a prompt cure in a few days, some even after only one treatment, though the most effective was application through very small cross-firing fields of 400 r daily to a total of 2,400 r with from 140 to 200 kv. The calcareous deposits disappeared in the acute, were not affected in the symptomless, and varied in those with mild or moderate symptoms, though the symptoms improved.

S. M. ATKINS, M.D.

Several Cases of Gonococcic Arthritis Treated by X-ray. M. L. Guillamet. Bull. et mém. Soc. de Radiol. méd. de France, October, 1937, **25,** 652–656.

Although x-rays have been successfully used in the treatment of gonococcic arthritis ever since 1904, they are not generally enough employed at the present day. The author presents a series of 21 cases treated with roentgen rays. He finds that in the majority there is an almost immediate amelioration of pain and swelling, and that hospitalization is considerably shortened and the arthritic sequelæ are markedly reduced. He advises a dosage of 200 r, given every few days as required by the duration of the disease. Certainly this method of treatment should be used more often as there is no doubt of the beneficial results.

S. R. BEATTY, M.D.

THE BLADDER

Treatment of Carcinoma of the Bladder by 400 Kilovolts Roentgen Therapy. A. H. Schumacher and David Steel. Ohio St. Med. Jour., October, 1937, **33,** 1116–1118.

In spite of the pessimistic attitude generally taken in regard to the treatment of carcinoma of the bladder by external irradiation, the authors feel encouraged by the survival of nine cases out of fifteen treated and quote favorable results from other clinics. The far advanced cases received only palliative treatment but those in better condition were given full doses ranging up to 14,000 r, equally divided over two anterior and two posterior ports. The factors used were: 400 kv. constant potential, 5 ma., 80 cm. distance, filter 0.93 mm. tin plus 0.27 mm. Cu plus an iometer chamber plus bakelite plus 2 mm. Cu built into the tube, giving a filter having the equivalent of 6.5 mm. Cu.

J. C. RODICK, M.D.

THE BLOOD

The Value of Determining the Reticulocytes in Examining the Personnel of Roentgen Laboratories. K. Mardersteig. Strahlentherapie, 1938, **61,** 279.

The author had an opportunity to examine the blood of employees of a roentgen tube factory. There were changes in the white blood picture, and occasionally an increase in the erythropoietic function which expressed itself in an increase of the reticulocytes or the hemoglobin and the erythrocytes. Chronic tonsillitis very often accompanied by pharyngitis and laryngitis was also found. This is chiefly due to the influence of ozone and nitrous gases; the described changes disappeared after the causative agents were removed. The author concludes that the determination of the reticulocytes is a reliable method for the recognition of bone marrow stimulation in persons working in x-ray laboratories.

ERNST A. POHLE, M.D., Ph.D.

BONE DISEASES (DIAGNOSIS)

Fibrocystic Disease and Hyperparathyroidism. J. Bauer and A. Jung. Rev. Chir., April, 1937, **75,** 284–295. (Reprinted by permission from British Med. Jour., July 31, 1937, p. 17 of Epitome of Current Medical Literature.)

The authors report an interesting case of a woman, 34 years of age, who complained of a violent pain in the right thigh and hip after a fall. A diagnosis of a neoplastic metastasis in the right femur was made roentgenographically, and roentgen therapy was given with some success. Two years later there were similar

pains in the left thigh, and both hips were treated by roentgen therapy with no result. There was a history of an early fracture of the right radius which had left a deformity, although function was good. Menstruation had not begun until the age of 20, and had now ceased. The patient was married, but she had no children. Radiological examination showed a generalized osteoporosis and the presence of numerous areas of bone absorption. These appearances suggested that the patient was suffering from generalized fibrocystic osteitis. Roentgenography showed the characteristics of fibrocystic disease, and laboratory tests confirmed this diagnosis. Although no parathyroid tumor could be seen or felt, it was assumed that there was one, and operation revealed a large adenoma in the region of the right inferior thyroid artery, which was removed. Pain disappeared after operation, but a spontaneous fracture occurred in the left femur and was put up in extension. The day after the operation the sign of Chvostek was seen, first on the left side of the face, then on the right, and there was paresthesia in the arms and leg. Gluconate of calcium was given intravenously and by the mouth. A typical attack of tetany developed, and there was a sudden alteration in the blood calcium content, which fell to 70 mg. the day after operation. Ammonium chloride was then given, and later a coffee of gluconate of calcium. The condition of the patient gradually improved and the fracture united satisfactorily. The authors consider that this case illustrates the influence of the parathyroid hormone on the osteoclastic resorption of bone.

Osteitis Deformans (Paget's Disease): Fissure Fractures—Their Etiology and Clinical Significance. M. Lowry Allen and Rutherford L. John. Am. Jour. Roentgenol. and Rad. Ther., July, 1937, **38**, 109–115.

Incomplete fissure fractures occur on the convex surface of the curved long bones of Paget's disease, particularly the femur and tibia. These follow slight trauma, since the bone is brittle. They heal with a minimum amount of bony callus which assumes the characteristics of the dominant Paget's disease. Additional slight trauma may result in complete fracture and, therefore, in patients with this disease one should be on the alert for fractures, which manifest themselves by sudden pain and a distinct persistent localized tenderness. Suitable splinting or bracing, with rest, should be instituted immediately.

S. M. Atkins, M.D.

Carbohydrate Metabolism Disturbance in Osteoporosis and Paget's Disease. R. C. Moehlig and S. Adler. Surg., Gynec. and Obst., April, 1937, **64**, 747–757.

These authors call attention to several points of similarity between osteoporosis and Paget's disease, namely, diabetic type of glucose tolerance curve, and high incidence of familial diabetes, familial obesity, and familial tallness. They attach great importance to this fact, since phosphorus compounds are essential to proper storage and utilization of carbohydrate. The controlling link between carbohydrate utilization and phosphorus lies in the pituitary gland, and therefore osteoporosis and Paget's disease have their etiology in some derangement of pituitary function. Evidence is given to substantiate the claim that the parathyroids do not participate in these two diseases. The authors also draw attention to the high incidence of goiter, fibroids, nephrolithiasis, and soft tissue calcifications including arteriosclerosis in patients suffering from osteoporosis or Paget's disease. In the treatment of these diseases, the authors recommend a measured diabetic diet together with the use of insulin, for long periods of time. Theelin injections have been used in an effort to check the activity of the pituitary gland, but with no success. Finally, they urge that dextrose tolerance and phosphatase studies be performed routinely in bone diseases.

H. A. Jarre, M.D.

A Clinical Pathological Contribution to the Study of Osgood-Schlatter's Disease. Sebastião Hermeto, Jr. Annaes Paulistas de Medicina e Cirurgia, September, 1937, **34**, 199–214.

The writer makes an extensive and rather complete histological study of two extirpated tibial tubercles. He states the symptoms of the condition known as Osgood-Schlatter's disease, the x-ray findings, and suggests treatment.

He recalls that Osgood, of Boston, and Schlatter, of Berlin, described the condition simultaneously in 1903. Both believed it to be traumatic in origin, the latter calling it a "fracture by traction," while Alsberg, in 1908, considered it to be inflammatory, and called it an "apophysitis." Axhausen believes it is an aseptic necrosis of the epiphysis, and suggests a common origin for this condition, Calvé-Legg-Perthes disease, Köhler and König disease.

To have a clear concept of the affection, knowledge of the development of the tibial tubercle is imperative. The work of Fromme, Müller, and Schultze, which showed the influence of disturbances of growth in anomalies of ossification is cited, and followed by the study of tissue slides made from two extirpated anterior tubercles presenting the affection known as Osgood-Schlatter's disease. After describing in detail the findings, the following conclusion is reached: Osgood-Schlatter's disease is an abnormal ossification of the tibial tuberosity—the abnormality usually assuming increased ossification of the cartilaginous process that projects into the insertion of the quadriceps tendon.

A. Mayoral, M.D.

BONE DISEASES (THERAPY)

Roentgen Therapy of Benign Bone Disease. W. Lahm. Strahlentherapie, 1937, **60**, 631.

The author discusses briefly his experience in the

treatment of benign disease by roentgen rays. Osteomyelitis, localized osteitis fibrosa cystica, giant-cell tumor, and osteitis deformans are included. Illustrative cases with roentgenograms are appended. One case of osteitis deformans of the pelvis and femur is interesting because the patient was unable to walk at the time of admission. He responded so well to roentgen therapy that he is now able to work from 10 to 12 hours and to walk without difficulty. In spite of this clinical improvement the roentgenogram shows no changes as compared with the findings before the treatment.

ERNST A. POHLE, M.D., Ph.D.

BREAST CANCER

Carcinoma of the Male Breast. Carl A. Kunath. Jour. Iowa St. Med. Soc., January, 1938, **28,** 10–13.

Six cases of carcinoma of the male breast have been diagnosed at the University of Iowa Hospitals in the last ten years. This is approximately 1.27 per cent of all breast cancers admitted during this period and corresponds closely to the incidence given by other authors. There is general agreement that breast cancer in the male has a much gloomier prognosis than in the female. The reasons for this are not clear but the author believes that the factor of late diagnosis due to failure of the medical profession to recognize that the disease exists in the male may play a large part. Pain has been reported to be the most common symptom in males and to occur earlier. Ulceration of the skin is more frequent, even in the earlier stages. The same is true of muscle involvement and fixation of the chest wall. In the author's six cases the first symptom noted was a mass. Pain was prominent in two cases but none had a discharge from the nipple or fixation to the chest wall; axillary node involvement was present in four cases; one gave a history of trauma preceding the development of a mass; microscopically, all were adenocarcinomas. It is generally agreed that the treatment should be the same as for the female, *i.e.*, radical amputation and irradiation. Of the six cases reported, only four survived the operation. Of these four, one is living and has a local recurrence, two died 14 and 17 months after operation, respectively, and one died two and one-fourth years later, probably from other causes.

L. W. PAUL, M.D.

CANCER (DIAGNOSIS)

Extensive "Radiologic" Defects Corresponding to Cancers Not Found by the Surgeon. M. R. A. Gutmann. Bull. et mém. Soc. de Radiol. méd. de France, October, 1937, **25,** 599–603.

The author describes several cases with large radiologic defects which were not demonstrable at operation. Such a defect may be a pseudo-tumor due to functional causes or a tumor such as a lymphoblastoma, which is of very soft consistency and not, therefore, palpable at operation. Sometimes edema from gastritis or gastric ulcer will produce large masses which cannot be found at operation but which disappear under proper treatment.

S. R. BEATTY, M.D.

CANCER (THERAPY)

The Biological Principles of Radiation Therapy of Malignant Tumors with Fractional Doses. J. Borak. Strahlentherapie, 1938, **61,** 63.

The author reviews the history of the development of the fractional dose method in roentgen therapy and points out that Freund, of Vienna, created the method, that Schwarz furnished the theoretical background, Regaud the experimental foundation, while Coutard used it in clinical practice.

ERNST A. POHLE, M.D., Ph.D.

Radiotherapeutic Five-year Results in Carcinoma of the Cervix Treated during 1930 as Published in the Communication of the Section on Hygiene of the League of Nations. H. R. Schinz. Strahlentherapie, 1938, **61,** 38.

In March, 1937, Heyman published on request of the radiological subcommittee of the League of Nations a statistical report giving the five-year end-results obtained in the treatment of carcinoma of the cervix during 1930 in six clinics. One was located in Brussels, one in Liverpool, two in London, one in Paris, and one in Stockholm. A total of 757 patients were observed; 89 per cent of these were treated. An average of 31 per cent were free from symptoms at the end of five years although the individual results of the six clinics varied from 17 (47 per cent). Schinz presents a critical analysis of these figures and attempts to explain the discrepancies in the end-results. He comes to the conclusion that neither the selection of the cases nor the error due to small numbers explains it. One might consider the influence of race and age. Furthermore the differences in the methods of radiation therapy should be studied: no data on these are given in Heyman's publication. He suggests, therefore, a comparison of the treatment methods used in the six clinics on whose records Heyman's report is based.

ERNST A. POHLE, M.D., Ph.D.

Indications for X-ray Therapy. H. Holfelder. Wien. klin. Wchnschr., July 16, 1937, **50,** 1051–1054. (Reprinted by permission from British Med. Jour., Sept. 18, 1937, page 41 of Epitome of Current Medical Literature.)

Holfelder gives the results of his extensive experience in the treatment of malignant growths with x-rays, and compares them with those obtained by operation. In small carcinomas of the skin surgery and irradiation give equally good results, whereas extensive inoperable skin carcinomas can be treated only by irradiation.

The proportion of recurrences in these cases was only 20 per cent. Of cases of inoperable carcinoma of the breast treated with x-rays, 40 per cent were alive after three years, and 36 per cent after five years. Prophylactic post-operative irradiation considerably improved the operative results; 68 per cent of cases treated in this way were alive after three years and 54 per cent after five years. Untreated bronchial carcinoma practically always proves fatal, but three cases treated with x-rays were alive after seven, six, and four and a half years, respectively. Similar results were obtained in cases of carcinoma of the esophagus, in the treatment of which the author prefers x-rays to intra-esophageal applications of radium. X-ray treatment cured 5.5 per cent of cases of inoperable carcinoma of the stomach, and an improvement was effected in 42 per cent of all the cases treated. In lymphogranulomatosis x-ray treatment considerably retarded the inevitable fatal issue. In pituitary tumors a clinical cure was obtained in 50 per cent of cases, and the author thinks that in spite of the excellent operative results treatment by irradiation is preferable in these cases. A five-year cure in cases of osteogenetic sarcomas was obtained in 23 per cent of cases by x-rays alone, and in 31 per cent by combined surgical and radiological treatment. The author stresses the importance of the collaboration between surgeon and radiologist in the treatment of malignant growths.

Six and One-half Years' Experience in Cancer Therapy with Ultra-hard Roentgen Rays. E. v. Schubert. Strahlentherapie, 1938, **61**, 97.

This is a brief report of the author's experience with 600 kv. roentgen rays in the treatment of 194 cases of malignant tumors seen from 1930 to 1935. He used a focal skin distance of 94 cm., 1.5 ma., 3.0 mm. Cu + 3.0 mm. Al, which delivered 3–4 r/min. The total treatment was concentrated on two or three days, with daily sittings lasting four or five hours. The distribution of the radiant energy within the pelvis and the efficacy of intra-uterine radium application as a supplementary method are discussed. An analysis of the cases indicates that supervoltage therapy with massive doses given within a few days leads to better results than exposure to a larger number of fractional doses. The author recommends 2,000 r (in air) given over two large fields within two days. The results with higher doses are less favorable. It is concluded that roentgen therapy with from 400 to 500 kv. has so many advantages that its general acceptance and use seem desirable.

ERNST A. POHLE, M.D., Ph.D.

Intravaginal X-ray Treatment. F. Erichsen. Zentralbl. f. Gynäk., June 5, 1937, **61**, 1330–1335. (Reprinted by permission from British Med. Jour., July 31, 1937, page 19 of Epitome of Current Medical Literature.)

The author is satisfied that he has had better results in the treatment of inoperable cervical carcinoma since he introduced, six years ago, a supplementary x-ray treatment by a Schaefer-Witte tube introduced into the vagina. Primary parametrial or secondary pelvic wall deposits are thus more accessible, and in contrast to radium treatment the use of a very high irradiation dosage is compatible with the protection of neighboring healthy tissues. The general scheme of treatment is: (1) radium, 4,000 to 5,000 mg.-hr. being given; (2) percutaneous x-radiation, 1,800 r being applied from four to six front, back, and side fields, and 800 r from a perineal field; this is alternated with (3) 1,600 to 2,000 r at a depth of 5 cm. directed to the right and left pelvic walls from the intravaginal water-cooled tube. Increase beyond the last-named dose is useless if not harmful, and the whole treatment occupies about 40 days. Disturbances of rectal and vesical function may follow, but no fistulæ developed; the lateral vaginal walls showed transitory appearances of membranous inflammation. In inoperable (Groups III and IV) patients thus treated, 38 per cent were living and symptom-free from one and a half to four years later, as well as three out of 12 patients who were treated for local recurrences.

Radiation Therapy in Advanced Malignant Disease. E. A. Pohle. Strahlentherapie, 1938, **61**, 233.

"The value of radiation therapy in advanced malignant disease is not sufficiently appreciated; it not only offers palliation in many instances, but occasionally one experiences surprisingly good end-results. Since there is no way of predicting which case will respond to radiation, it should be tried wherever possible, even in relatively hopeless cases. A brief report is made of a series of cases selected at random to illustrate the author's experience in treating advanced malignant neoplasms by roentgen rays. Although the patients discussed here have received only this type of radiation, it is emphasized that radium also has its place in this field. Other radiologists are urged to publish similar material which has come under their observation."

AUTHOR

THE CHEST

Triangular Para-apexian Shadow. P. Cossio and A. Trimani. Revista Argentina de Cardiologia, July-August, 1937, **4**, 157–169.

After discussing the causes assigned by other workers for the triangular shadows occasionally observed in the cardiophrenic angles in roentgenograms of the thorax, the authors report their findings and conclusions based on the study of teleroentgenograms and orthodiagrams made of the chests of 3,968 individuals and anatomical observations postmortem of 20 specimens.

In this material the para-apexian shadow was found 57 times, mostly in the male, and not once in an individual below the age of thirty. Roughly, 75 per cent of the persons in whom the sign was found were of the lean or normal weight type. In 78 per cent some car-

diac lesion was found, while in 22 per cent there were no lesions. In no case showing cardiac lesions with marked enlargement was the sign found.

Based on autopsy findings the authors believe that the triangular para-apexian shadow is due to a ligament extending from the dome of the left leaf of the diaphragm to the lower part of the parietal pericardium, the presence of fat being only contributory.

A. MAVORAL, M.D.

Roentgen Kymographic Study of the Phenomenon of Kienböck. P. Thoyer-Rozat and Jacques Bernard. Jour. de radiol. et d'électrol., November, 1937, **21,** 499–502.

The authors have studied the phenomenon of Kienböck with the kymograph and have demonstrated that the paradoxical movement of the fluid level of hydropneumothorax is due to shift of the mediastinum rather than to paralysis of the diaphragm.

S. R. BEATTY, M.D.

COLITIS

A Review of Idiopathic Ulcerative Colitis, with Report of Five Cases. Jonas C. Kopelowitz. Jour. Missouri St. Med. Assn., February, 1938, **35,** 41–48.

The recent literature on ulcerative colitis is reviewed with special reference to etiology, symptomatology, and treatment. Many organisms have been incriminated but especially the *B. dysenteriæ*, Bargen diplostreptococcus, and the *B. coli*. Many workers—and there is a definite trend toward this view—feel that ulcerative colitis belongs to the dysentery group. Bargen has been the chief exponent of the diplostreptococcus, but his views have not found universal acceptance. The theory of an avitaminosis has some supporters since ulcerative colitis has a close resemblance to sprue and pellagra.

Concerning incidence, ulcerative colitis shows no seasonal variations and affects both sexes equally. The disease is most common between the second and fourth decades, with the average age about thirty. The duration varies from a week to twenty years or longer.

Symptomatically, cases may be divided into three groups: (1) The non-toxic, non-sclerotic with no evidence of toxemia or systemic manifestations; (2) the non-toxic, sclerotic, with marked permanent changes to colon and rectum, with rigid contracted and stenosed bowel from long standing colitis; (3) the toxic, with septic fever, leukocytosis, anorexia, nausea, vomiting, rapid pulse, and prostration. This group includes those cases with rapid onset in which no treatment seems to be of avail (about 5 per cent of all cases).

Many forms of treatment have been advocated. This should include rest in bed during the acute stage, outdoor régime when improved, sunlight, and ultraviolet light to the abdomen. The diet should be one with a low residue and with a caloric value of about 3,000 per day. Vitamins should be given, either as a concentrated preparation or in the form of orange juice, tomato juice, butter, and yeast. A wide variety of oral, rectal, and intravenous medicaments have been advocated.

The results of surgical treatment are not encouraging. Conservative surgery, preferably ileostomy, is indicated if medical management fails to control the symptoms. It is recommended, also, in the presence of massive hemorrhage, persistent fever and rapid pulse, persistent nausea and vomiting, or continued bloody diarrhea not improved by repeated blood transfusions. In the author's series of 34 cases, operation was done in six with three deaths. There were four other deaths without surgery, a total mortality of 20 per cent.

Five typical cases are summarized and illustrative roentgenograms are included. A bibliography of 50 articles, mostly of the more recent literature, is appended.

L. W. PAUL, M.D.

CONTRAST MEDIA

Acute Bismuth Poisoning, with Recovery. N. M. Keith and A. E. Osterberg. Arch. Int. Med., September, 1937, **60,** 415–423.

Two cases of acute bismuth poisoning are presented, resulting from cystographic injection of an alkaline solution of bismuth and potassium tartrate. Onset symptoms were characterized by rapid development of oliguria or anuria within from 24 to 48 hours, accompanied by nausea and vomiting. Stomatitis and bleeding from the gums developed three or four days after the onset. Characteristic blue-black discoloration of gums and mucous membranes did not appear until several days later. There was a marked rise in concentration of blood urea and creatinine, and a decrease in the bicarbonate reserve and chloride concentration of the plasma.

Treatment consisted of intravenous injection of 1 per cent sodium chloride, from 5 to 10 per cent dextrose, and 5 per cent sodium bicarbonate, daily injections totalling from 1,000 to 3,000 c.c. In one of the cases sodium thiosulphate did not appear to affect the toxemia.

The authors point out the similarity between bismuth toxemia and that produced by other heavy metals, especially mercury bichloride. In lead poisoning, renal insufficiency does not occur.

H. A. JARRE, M.D

THE CRANIUM

Intracranial Projectiles. M. Alfred-Lévy. Bull. et mém. Soc. de Radiol. méd. de France, October, 1937, **25,** 630–635.

The author presents two cases in which bullets inside the cranium migrated downward and backward toward the base. He believes that the weight of the lead bullets is the determining factor in this migration.

S. R. BEATTY, M.D.

DEFICIENCY DISEASE

Clinical Course and Treatment of Sprue. D. K. Miller and W. H. Barker. Arch. Int. Med., September, 1937, **60,** 385–414.

The authors present a review of 33 cases of sprue studied during the past four and a half years. The cases are classified according to symptoms at the time of entrance to the hospital. Severe cases had anemia and diarrhea, moderate cases had diarrhea but no anemia, and mild cases had neither diarrhea nor anemia. All cases gave a history of having had typical sprue symptoms. Recurrent attacks of distention or diarrhea had occurred in all cases over periods varying from one to nine years.

Of these cases, 29 were studied roentgenographically. The outstanding findings were: (1) a variation in the caliber of the intestinal segments; (2) a distortion of mucosal pattern, usually of the jejunum, but often of the duodenum and ileum, and (3) a segmental distribution of barium, probably produced by abnormal motility of portions of the small bowel. The authors emphasize that, while these findings were constant in all cases investigated roentgenographically, such manifestations cannot be regarded as pathognomonic of sprue. They are probably due to improper fat absorption in the small intestine.

Treatment resulted usually in marked amelioration of symptoms. The treatment consisted of: (1) rest in bed; (2) high protein, low fat, low carbohydrate diet; (3) parenteral liver extract.

H. A. Jarre, M.D.

DIATHERMY

Measurements on Biological Phantoms with Very Short Waves of Great Energy. J. Pätzold. Strahlentherapie, 1937, **60,** 700.

The author studied the effect of various wave lengths on fat and muscle. For the 6-meter wave the temperature ratio was 16:1 and for a 1-meter wave, 3:1. This would indicate that the 1-meter wave is preferable, especially for heating the pelvis, because the difference in the heating of fat and muscle is much less than for longer waves.

Ernst A. Pohle, M.D., Ph.D.

DIPHTHERIA CARRIERS

The Use of Roentgen Rays in Diphtheria Carriers. W. Streil. Strahlentherapie, 1938, **61,** 130.

The author used roentgen therapy in 150 cases of diphtheria carriers. Technic: 150 kv., 4 ma., 0.25 mm. Cu + 1.0 mm. Al, 6–8 fields over the nasal area and over both tonsils, 50 r per field. The first smear was taken two or three days after the exposure and then from four to six days later. If the second smear was reported positive, the second and sometimes the third exposure was given. The patient was discharged after three negative smears had been reported. The treatment was successful in 95 per cent of the patients who excreted bacilli and in 97 per cent of those who were carriers. Because of the good results obtained and the economical advantages, roentgen therapy of diphtheria carriers is recommended by the author.

Ernst A. Pohle, M.D., Ph.D.

Radiotherapy in Diphtheria Carriers. Laquerrière, Kuentz, and Roget. Bull. et mém. Soc. de Radiol. méd. de France, October, 1937, **25,** 681, 682.

The authors describe their experience in the treatment of 17 cases of diphtheria carriers with success in curing every case. Technic: 100 r with 5 mm. Al filtration at 125 kv. They gave one treatment every three or four days. From two to four treatments usually were sufficient. They believe the method should be used in every case in which the usual methods of treatment do not clear up the nasopharynx of the diphtheria carrier.

S. R. Beatty, M.D.

DOSAGE

The Determination of the Dose in Radium Therapy of Carcinoma of the Cervix. J. J. Hirsch, Strahlentherapie, 1938, **61,** 48.

The author undertook a comparative study of the methods of radiation therapy for carcinoma of the cervix as practised at the Curie Institute in Paris and the Radiumhemmet in Stockholm. At the present time there is no direct relationship between the amount of radium applied and the tissue dose. He believes that this can be established as soon as radium doses can be expressed in international r. The photographic method developed by Holthusen and his school seems to be a suitable method to reach this goal. The comparison of the doses in the small pelvis with the Paris and Stockholm methods showed that there is a rapid drop of the intensity toward the parametria. It seems necessary, therefore, to supplement the intra-uterine radium application by external irradiation.

Ernst A. Pohle, M.D., Ph.D.

Dosage Measurements on Ten 400-kilovolt Roentgen-ray Generators. Otto Glasser. Am. Jour. Roentgenol. and Rad. Ther., November, 1937, **38,** 769–775.

There was found but remarkably slight variation in the quality and quantity output of the same types of 400 kv. generators, using General Electric (XPT_4) tubes, when tested by the author.

Ten units were examined: six were of the pulsating potential and four of the constant potential. In six installations the tubes were suspended in air, and in four they were immersed in oil. The radiation from the oil-immersed tubes is somewhat softer than that produced by tubes suspended in air. The highest output in roentgens per minute was produced by a constant potential unit with the tube immersed in oil.

The half value layers in copper for the 400 kv. ranged from 3.6 mm. to 5.2 mm., compared with 1.1 mm. for 200 kv. Depth doses for 400 kv. with different field sizes at 50 cm. focal distance showed a considerable difference, but at 80 cm. somewhat less. Back-scattering at 400 kv., even for large areas, was slightly more than 20 per cent as compared to over 40 per cent for 200 kv.

S. M. ATKINS, M.D.

Certain Conclusions from Study of Radiation of 200–400 Kilovolts with the Photoelectric Cell. André Denier. Bull. et mém. Soc. de Radiol. méd. de France, October, 1937, **25,** 651, 652.

The author has made a study of the effects of x-rays on the reading of the photoelectric cell in the region from 200 to 400 kv. He finds that below 0.15 Å. the sensibility falls rapidly toward the region 0.083 Å. There is a sharp drop between 0.10 and 0.150 Å. which is of interest in that it may allow a means of measuring quality of a given radiation in this range but makes the instrument unsatisfactory as a measure of quantity. With a given quality of ray a remarkable proportionality of the current with the intensity of irradiation exists which can be verified by changing the distance only and applying the law of the square root.

S. R. BEATTY, M.D.

Roentgen Caustic: Its Principles and Application. G. J. van der Plaats. Strahlentherapie, 1938, **61,** 84.

The author suggests the term "roentgen caustic" for the method of applying roentgen rays at relatively low potentials, short focal skin distance with high intensities, and large doses. This method has been developed during the last few years by Chaoul and his co-workers. The principles of the method are discussed at length; its great advantage is the rapid drop of the dose from the surface toward the depth. If it is not desirable to preserve the integrity of the skin, unfiltered radiation at the shortest possible distance is the method of choice. A special apparatus which permits irradiation at 50 kv., no filter, 2 cm. F.S.D., is described and its advantages in focusing the beam on the lesion demonstrated.

ERNST A. POHLE, M.D., Ph.D.

Coördination of Physical and Biological Dosage in High Voltage and Supervoltage Roentgen Therapy. T. Leucutia and K. E. Corrigan. Am. Jour. Roentgenol. and Rad. Ther., November, 1937, **38,** 762–768.

It is recommended that the physical dose be always coördinated with the biological dose when prescribing a certain radiation treatment.

For the present, the skin erythema still appears as the most suitable biological indicator, and therefore it is recommended that it be used routinely as a biological dose unit. Since with increasing voltages an increasingly larger physical dose can be administered to produce a similar erythema, a curve expressing this relation will be of great clinical aid. This type of curve may serve as a basis for the derivation of other curves, such as, for example, the curve expressing the measurement of roentgens in free air, equivalent curves for various size fields by taking into consideration the surface scattering, curves expressing the time factor when treatment is fractionated and protracted, etc.

The physical dose should always include a statement of (*a*) the quality of the radiation, expressed in the form of a complete absorption curve describing the equivalent voltage or half value layer; (*b*) the quantity of the radiation expressed in roentgens, measured in free air with a thimble chamber; (*c*) the intensity factor (r/min.), and (*d*) the time factor, or daily loss of radiation effect, if treatment is extended over a certain length of time. Finally, it should include a detailed description of all factors pertaining to technic, such as radiation source, calibration, and clinical procedure.

S. M. ATKINS, M.D.

Roentgen Therapy with Supervoltage in North America. O. Glasser. Strahlentherapie, 1937, **60,** 557.

The author describes several of the supervoltage installations in this country and briefly discusses some of the problems in dosimetry.

ERNST A. POHLE, M.D., Ph.D.

Principles of Dosimetry in Radiation Therapy by the Rotation Method. R. du Mesnil de Rochemont. Strahlentherapie, 1937, **60,** 648.

The author investigated the various factors affecting dosage in irradiation with the rotation method (see also paper by Dessauer, same journal, 1937, **60,** 546). Numerous mathematical deductions are given showing the relation between focal skin distance, field size, and surface and depth doses. The differences in the isodose curves as compared with those obtained when patient and tube are immobilized are also shown. Blanks are reprinted which permit the recording of the doses in practice.

ERNST A. POHLE, M.D., Ph.D.

THE ESOPHAGUS

Esophageal Varices. Albert Oppenheimer. Am. Jour. Roentgenol. and Rad. Ther., September, 1937, **38,** 403–414.

The roentgenologic appearance of esophageal varices is the product of two variable factors, namely, anatomical formation and actual physiological condition during exposure.

Anatomically the roentgen findings vary with the stage of the disease. The early stage, marked by a slight and diffuse congestion, results in moderate broadening of the rugæ of the lower esophagus. The beginning of the dilatation of the large veins results in small rounded defects of the lower fifth of the esophagus. The generalized enlargement of numerous veins

results in the typical vermiform negative shadows. Variations in the size and shape of the veins, as produced by the phase of the respiration, peristalsis, stripping and mechanical pressure, cause a change in the picture. In the early stages, owing to pressure by bolus and peristalsis, the blood is pressed into abdominal vessels and thus varices cannot be demonstrated, and only a slight delay or widening of the lower esophagus from functional failure of the cardia to open is seen. In the terminal stages also, stasis is noted.

The method of examination is the oblique recumbent position, at the end of full inspiration (veins filled), and five seconds after swallowing a very small amount of a thick barium preparation that will demonstrate mucosal folds. Air bubbles can be excluded by films in various positions. Fluoroscopy is not very helpful.

S. M. Atkins, M.D.

Pharyngo-esophageal Diverticulum: Analysis of 53 Consecutive Operative Cases. F. H. Lahey and W. B. Hoover. New Eng. Jour. Med., April 8, 1937, **216**, 591–597. (Reprinted by permission from British Med. Jour., Aug. 7, 1937, page 23 of Epitome of Current Medical Literature.)

The authors analyze 53 consecutive cases of operation for diverticula of the lower pharynx and upper esophagus. Of these cases, 43 were men and ten women. The outstanding symptoms of this condition are difficulty in swallowing, regurgitation, gurgling noises, choking attacks, and loss of weight. The diagnosis can usually be made from the clinical history, but should be confirmed by a careful roentgenologic study. The x-ray examination also rules out other lesions of the esophagus and ascertains the size, shape, and position of the sac. The operation for such diverticula is done in two stages. At the first operation the sac in the neck is completely freed, the encircling constrictors are carefully dissected and cut, and the dome of the diverticulum is then fixed high in the wound, so that it lies at a higher level than the opening into the esophagus. This operation relieves the patient's symptoms at once; the second one takes place from eight to 12 days later, and the sac is then amputated. The authors recommend a special dissection of the mucosa from the submucosa; a small cuff of mucosa is pushed into the neck of the sac and the submucosa sewn over it, and in this way leakage can practically always be avoided. Most of the patients require post-operative dilatation and this must often be continued for a year. In the authors' series good results were obtained in 49 cases, poor results in two cases, and two were failures.

Cardiospasm. E. K. Frey and L. Duschl. München. med. Wchnschr., Aug. 27, 1937, **55**, 1374–1377.

There is considerable discussion as to the true nature of this condition, and this is exemplified in the various terms employed in describing this entity; thus, "hiatus spasm" is definitely a misnomer, as is the term "cardiospasm." "Dysphagia paradoxa" reveals nothing as to the etiology of the condition. "Achalasia," or absence of relaxation, has much in its favor, though all observers are not in accord with this explanation of the *modus operandi*. "Idiopathic dilatation of the esophagus" or other similar names only attest to our ignorance of the subject, and probably should never be used. Starck is quoted as considering the entity as one of cardiotonic dilatation of the esophagus. Roentgenologically, the condition is observed to vary from mere cylindrical dilatation to actual mega-esophagus. It is very possible to have a pathologic narrowing of the esophagus without proximal dilatation.

In what is commonly considered a typical case, at the site of narrowing the pathognomonic conical tapering is observed toward the cardia. The swallowing function, filling and emptying of the esophagus, are essential in diagnosing early cases, and it is imperative to obtain roentgenograms in both oblique projections. A rather detailed account of all the varied theories offered to explain this entity are briefly and well presented. In summary, these are possible; congenital basis, absence of relaxation reflex, true spasm, inability of efficient contraction of longitudinal esophageal musculature, primary atony after infectious diseases or trauma, disharmony of autonomic and sympathetic nervous systems, and psychic trauma. These theories explain the efficacy of such divergent therapeutic procedures as: auto-suggestion and hypnosis, atropine and other antispasmodics, dilatation, sympathectomy, esophageolysis, cardiomyotomy, cardioplasty, and esophago-gastrostomy.

W. R. Stecher, M.D.

Notes on the Roentgen Picture of the So-called Esophagus Lip. Gunnar Jönsson. Acta Radiologica, May, 1937, **18**, 452–459.

The author points out that in making a roentgen examination of the hypopharynx and the upper part of the esophagus, there is now and then observed a rounded bulging in the posterior wall immediately below the cricoid cartilage. This bulging has been said to depend on a swelling of the mucous membrane caused by a foreign body. The author, however, has noted that normally one not infrequently observes a bulging on the border between the hypopharynx and the esophagus, that this bulging corresponds to the so-called esophageal lip demonstrated by Killian and that it probably results from the lower part of the musculus cricopharyngeus, which acts as a sphincter muscle in the esophageal mouth. The part played by the mucous membrane in this bulging requires further investigation.

W. A. Sodeman, M.D.

Traction Diverticulum of the Esophagus: Roentgenographic Demonstration: Symptoms Noted in Series of 26 Patients. R. P. Wallace. Arch. Int. Med., September, 1937, **60**, 454–457.

Although traction diverticula are usually considered

to occur without symptoms, the author presents an analysis of 26 cases discovered roentgenographically, ten of which had symptoms directly traceable to the diverticulum. Substernal pain was present in six cases. Dysphagia, distinct from substernal pain, was experienced by six patients. Hematemesis occurred in three cases. Other minor symptoms were eructations, simple vomiting, hiccup, pain in the epigastrium, and weakness. There was no relationship between the size of the diverticulum and the occurrence of symptoms.

H. A. JARRE, M.D.

FISTULA

Chronic Pararectal Fistula Treated with X-ray Therapy: Ten-year Cure. Th. Nogier. Bull. et mém. Soc. de Radiol. méd. de France, October, 1937, **25,** 645, 646.

A persistent sinus tract which had been treated surgically for a period of over ten years was irradiated by the author with fairly heavy doses of x-ray through 5 mm. Al filter. A total dose of 4,800 R (Solomon) was given. The lesion has remained healed for 10 years. There is atrophy and telangiectasis of the region, but the skin is supple and unbroken.

S. R. BEATTY, M.D.

FOREIGN BODIES

Unusual Foreign Body in Esophagus and Stomach. E. Oppikofer, Jr. Schweiz. med. Wchnschr., Jan. 1, 1938, **68,** 26, 27.

After Toni, the Vienna "house-breaking king," was arrested he tried to commit suicide by swallowing a piece of wire and 39 pins. Within the next five days, 32 of the pins were evacuated, but it was necessary to remove the piece of wire by esophagoscopy from its location half in the esophagus, half in the stomach.

LEWIS G. JACOBS, M.D.

GALL BLADDER (NORMAL AND PATHOLOGIC)

Newer Developments in Cholecystography. E. N. Collins and J. C. Root. Cleveland Clin. Quart., April, 1937, **4,** 85–97. (Reprinted by permission from British Med. Jour., Aug. 14, 1937, page 27 of Epitome of Current Medical Literature.)

In an attempt to standardize procedure in the newer developments of cholecystographic examination, Collins and Root point out the following features: It has been found that the administration of multiple doses of the dye produces greater density in the visualized gall bladder than does a single dose, and it makes nonvisualization of greater significance and it does not harm the patient. The administration of large amounts of sugar and other carbohydrates, before and during examination, facilitates the excretion of the dye by the liver. One ounce of a mixture of egg yolk, lecithin, and glycerin is as efficacious in emptying the gall bladder as the fat meal. The use of pitressin in eliminating confusing shadows in the intestinal tract which lies over the area of the gall bladder has precluded the necessity for re-examination. It has also made the multiple dose oral method of cholecystography possible on the same day that barium meal examinations of stomach and small intestine, or barium enema examinations of the colon, are made. In a series of 1,250 cholecystographic examinations, pitressin was used in 200 cases, and effective results were obtained in 87.5 per cent of these. In a more recent series, in which the new ampule containing 20 pressor units was used, effective results were obtained in 90 per cent of cases. Diagnosis in these cases is usually simple when there is a history of biliary colic, especially if associated with jaundice, and it may be confirmed by cholecystography. In inflammatory diseases of the gall bladder physical examination is of assistance only during the acute or subacute stages. The authors observe that during the last five years the operative findings have coincided with the cholecystographic either positively or negatively in 95 per cent of cases.

A Probable Cause for the High Mortality Following Cholecystostomy, Cholecystogastrostomy, and Cholecystoduodenostomy in Jaundiced Patients. R. Russell Best and N. Frederick Hicken. Surg., October, 1937, **2,** 566–574.

Operations to relieve blockage of the common duct in the face of increasing jaundice are frequently unsatisfactory and carry a high mortality rate. One cause may be, the authors state, that anastomosis between the gall bladder and stomach or duodenum to relieve hepatic pressure may prove inadequate because the cystic duct may not be patent.

Probing the cystic duct or a study of the bile secretion has not proved to be reliable. Cholangiograms are used by the authors, either at the time of operation or after a cholecystostomy.

If done at the time of operation, the bile is aspirated and about 30–50 c.c. of iodized oil injected (or 48 per cent hippuran) and an x-ray film made with a portable apparatus. If contrast medium is seen in the common duct, a cholecystogastrostomy or cholecystoduodenostomy may be done. If none is seen, a choledochostomy or choledochoduodenostomy is indicated.

J. E. WHITELEATHER, M.D.

GENITO-URINARY TRACT (DIAGNOSIS)

Urethrography. J. H. Oltramare and R. Martinet. Schweiz. med. Wchnschr., Jan. 1, 1938, **68,** 12–25.

After a brief résumé of the methods of urethrography, the authors describe their usual technic. A catheter with a balloon bulb on the tip is inserted into the meatus and inflated until tight: 40 per cent lipiodol is then injected to fill the urethra. Two films are made, one posterior and one lateral. If one avoids pain in injection, no accidents are encountered.

The anatomy of the urethra is briefly reviewed. The x-ray image of the normal urethra has certain fixed

characteristics. The anterior portion, lacking muscle, is ballooned out to a cylindric canal. Some resistance is encountered in injecting the muscle-containing membranous urethra. Spasm of the muscle may lead to emptying of this portion if the film is taken after the injection. The anterior urethra has sharp borders. These are parallel in the penile portion but show enlargement into the bulbar dilatation below the symphysis. The posterior urethra is a narrow band showing an oval swelling at the prostate, in the center of which is a clear spot. The bladder neck appears as an estuary preceding the prostatic urethra. Some variation in appearance with age occurs.

Urethral strictures give a characteristic sharp narrowing of a normally dilated portion of the canal; they are to be distinguished from spasm by the fact that the latter is most frequent in the region of the membranous sphincter. Crypts and diverticula are well demonstrated, and always pathological. Demonstration of the glands of Littré and Cooper and the crypts of Morgagni never normally occurs. Prostatic crypts may be shown. A globular dilatation of the prostatic sinus is generally due to an old gonorrhea. Disappearance of the "spot" of the verumontanum indicates prostatic hypertrophy, as do displacements of the canal. The most characteristic sign of this condition, however, is saber-blade deformity of the urethra (Chevassu's sign). Deformity of the bladder may also be shown.

Trauma may lead to complete severance of the urethra, marked by a sudden end of the injected medium, to stricture, or to angulations without stricture.

Gonorrhea may lead to stricture, peri-urethral abscess, fistula, or changes in the prostate. In stricture, radiography is of great value in demonstrating the exact extent of the lesion, which cannot be shown in any other way. It is also a helpful check on treatment. Abscesses and fistulæ are best delineated by urethrography. Prostatic abscess in the early stage causes displacement of the urethra, while, after spontaneous evacuation, a fistula is formed. Chronic prostatitis may lead to abscess cavities in this gland, single or multiple. The x-ray signs of diffuse prostatitis are indefinite, but the distinction from cancer is important. The presence of multiple cavities with or without stones is a differential point. In old prostatitis obliteration of the verumontanum may occur.

Tuberculosis leads to very destructive lesions, especially in the prostate, often with reduced bladder capacity.

Prostatic hypertrophy leads to deformity of the canal, lengthening, change of direction, flattening of the transverse diameter, and deformity of the bladder neck. The verumontanum is always effaced. The saber-blade deformity is shown on oblique views. The normal muscular activity of the posterior urethra is lost. In cases without clinical enlargement the urethrogram may show changes to be present.

Cancer of the prostate produces variable signs: deformity, infiltration or edema of the walls, or elevation of the bladder floor

Post-operative studies show that cystotomy has no effect on the urethral obstruction due to prostatic enlargement. Study after prostatectomy shows that the bladder neck is reformed by the fourteenth day. A triangular dilated midsegment of the urethra occupies the site of the excised gland.

The article is a beautifully illustrated and careful review, well worth reading.

LEWIS G. JACOBS, M.D.

Gravel in the Kidney and Ureter. G. Marion. Jour. Urol., April, 1937, **43**, 297–303. (Reprinted by permission from British Med. Jour., Aug. 14, 1937, page 25 of Epitome of Current Medical Literature.)

Marion records five cases in which gravel in the kidney or ureter caused partial or complete obstruction. It is suggested that post-operative anuria may sometimes be due to obstruction of the renal tubules by crystals which are formed after certain operations on the urinary tract. The formation of gravel in the ureter is usually followed by its spontaneous passage, and this may be unnoticed if the patient possesses both kidneys, but when one has previously been removed anuria may be produced, and two instances of this are described. Gravel in the pelvis of the kidney gives rise to the same symptoms as calculus, and in some cases the gravel fills the whole of the pelvis and calices. Sometimes it is passed as a result of medical treatment; an instance is given of a young girl in whom radiography showed a stone the size of a bean, while an earlier film had shown it to be coral-shaped and much larger. It was established that, in the first x-ray plate, what appeared to be a large branching calculus was really gravel which had passed in the interval between the taking of the two films. Pyelotomy was later carried out for the removal of the stone. Any variety of lithiasis may give rise to this gravel formation, and in three cases in which the deposit was analyzed it was found to consist of oxalates, urates, and phosphates. A correct diagnosis cannot always be made by radiography, but when anuria is present and no stone can be seen gravel should be suspected. In this case, as when a stone is present, the treatment consists of ureteral catheterization, followed by surgical intervention if the gravel or stone is not passed and the obstruction relieved.

Calcification of a Bladder Infected with Bilharzia: Dilatation of the Uterus and Implantation of Tumor. P. C. Smyrniotis. Jour. de radiol. et d'électrol., November, 1937, **21**, 489–493.

The author presents a case of calcified bladder infected with bilharziasis which was diagnosed from the plain films. The ureters were thickened and calcified. There was no insufficiency of the ureters and the tonicity of the bladder was normal. The author believes that the bladder does not always hypertropy or calcify in this condition, neither is cancer formation more fre-

quent in bilharziasis than in the normal. The implantation of cancer in these cases, therefore, seems more directly connected with calcification.

S. R. BEATTY, M.D.

The Infant and Child as a Urologic Problem. E. Halsell Fite. Jour. Oklahoma St. Med. Assn., November, 1937, **30,** 391–397.

The author gives the indications for a complete urinary study in children, and points out the superiority of retrograde over intravenous pyelography. Several cases are presented.

JOHN M. MILES, M.D.

GENITO-URINARY TRACT (THERAPY)

Bilateral Hydronephrosis: 12 Cases. H. Smagghe. Jour. d'urol., January, 1937, **43,** 5–33. (Reprinted by permission from British Med. Jour., May 29, 1937, p 85 of Epitome of Current Medical Literature.)

The author, in discussing cases of bilateral hydronephrosis, states that the condition is not uncommon and is usually revealed by intravenous urography. Bilateral hydronephrosis is met with in cases of congenital malformation, in lesions of the lower urinary tract, causing obstruction in the bladder, prostate, or urethra, or in inflammatory lesions or tumors in the adjacent pelvic organs. These latter conditions bring about uretero-pelvic dilatation, but congenital lesions, of which the most common are abnormal vessels, cause a dilatation of the pelvis alone. Pelvic lesions, which may cause bilateral dilatation of the ureters, are most often found in women, and include prolapse of the uterus, uterine fibromas, and ovarian cysts. Certain cases of bilateral hydronephrosis show few symptoms, particularly those cases of congenital uretero-pelvic dilatation of primary origin. In other instances the dilatation causes indefinite feelings of heaviness in the lumbar region; in pregnancy this symptom is hard to distinguish from muscular fatigue. In typical cases pain may be persistent or intermittent, with crises similar to attacks of renal colic, affecting most severely the side on which the kidney is most damaged. The increase in size of the kidneys, being bilateral, may suggest polycystic disease, but the diagnosis can be settled by pyelography.

Prognosis in cases of bilateral hydronephrosis is grave, as progressive renal insufficiency leads inevitably to uremia. In pregnancy, if symptoms occur before the fourth month, the pregnancy should be interrupted. At a later stage drainage by ureteric catheters may be carried out, or in severe cases nephrostomy may be necessary. Nephropexy is indicated in all cases of simple pelvic dilatation after division of the abnormal vessel or adhesions, and also when the dilatation is of uretero-pelvic origin. In cases of infective dilatation nephrostomy should be carried out and the kidney allowed to drain for several months. Twelve cases of hydronephrosis are reported.

GRENZ RAYS

Methods for the Marking and Adjusting of Skin Areas in Grenz-ray Therapy. A. Kreiner. Strahlentherapie, 1937, **60,** 619.

The author describes his method for adjusting skin fields in Grenz-ray therapy. He uses a special focusing device which facilitates the reproduction of certain angulations. The fields are marked on the skin, numbered, and then photographed to allow accurate control of dosage and avoid overlapping of treated areas.

ERNST A. POHLE, M.D., Ph.D.

Our Experience with Grenz-ray Apparatus and Dosage Meters. H. Decker and J. Port. Strahlentherapie, 1937, **59,** 539.

The authors examined a number of pieces of apparatus for the production of Grenz rays, including filters, and also undertook a series of measurements with the dosage meters available for the calibration of such apparatus. They found a number of shortcomings in the construction of the apparatus and offer suggestions for remedying them. Some of the dosage meters showed differences as high as 25 per cent and they conclude, therefore, that the instruments on the market at present are not suitable for accurate measurements in the Grenz-ray region.

ERNST A. POHLE, M.D., Ph.D.